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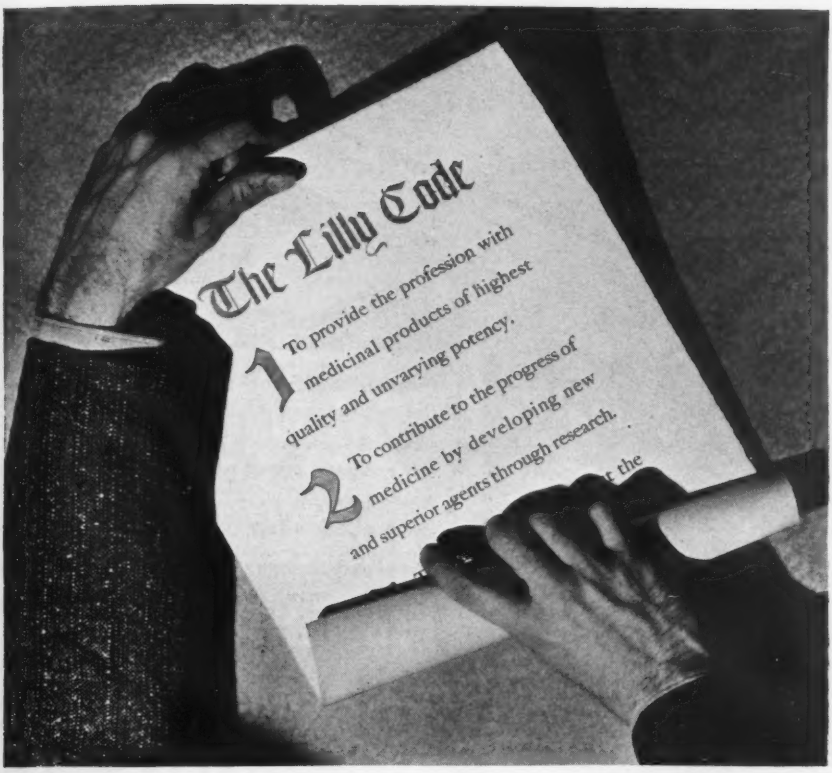
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1. Am. J. Obst. & Gynec. 39:82, Jan. '40

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1 Jr. Biol. Chem., Dec., 1919
2 Pub. Health Reports, Jan., 1925
3 Jr. A.M.A., March 13, 1937
4 Am. Jr. Dis. Children, Oct., 1923
5 "Vitamin B_1", 1938, p. 133

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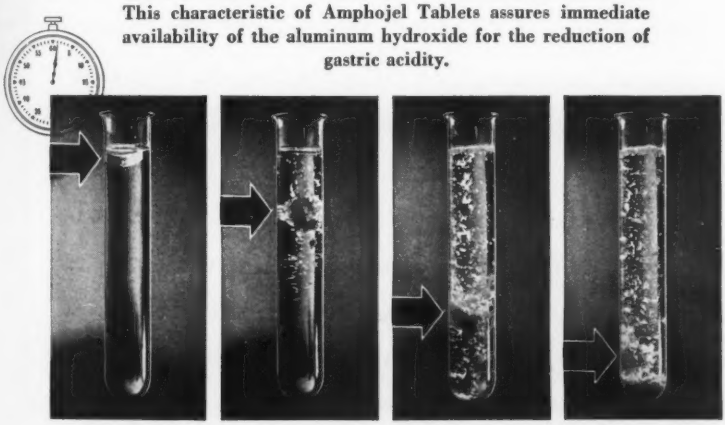

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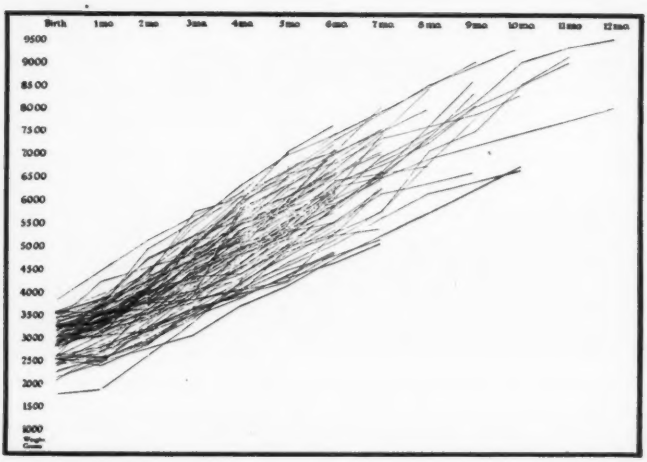

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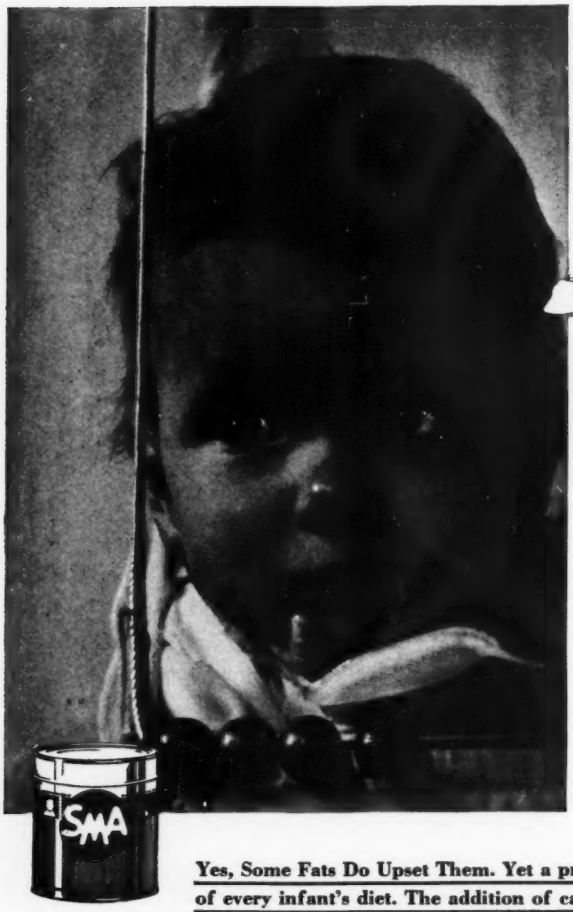

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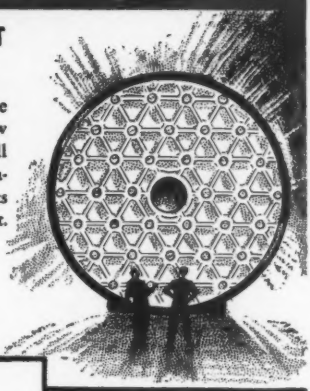

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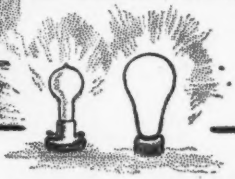

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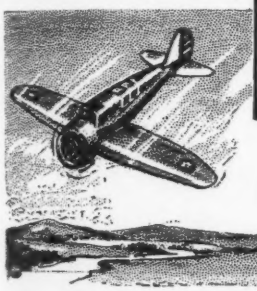

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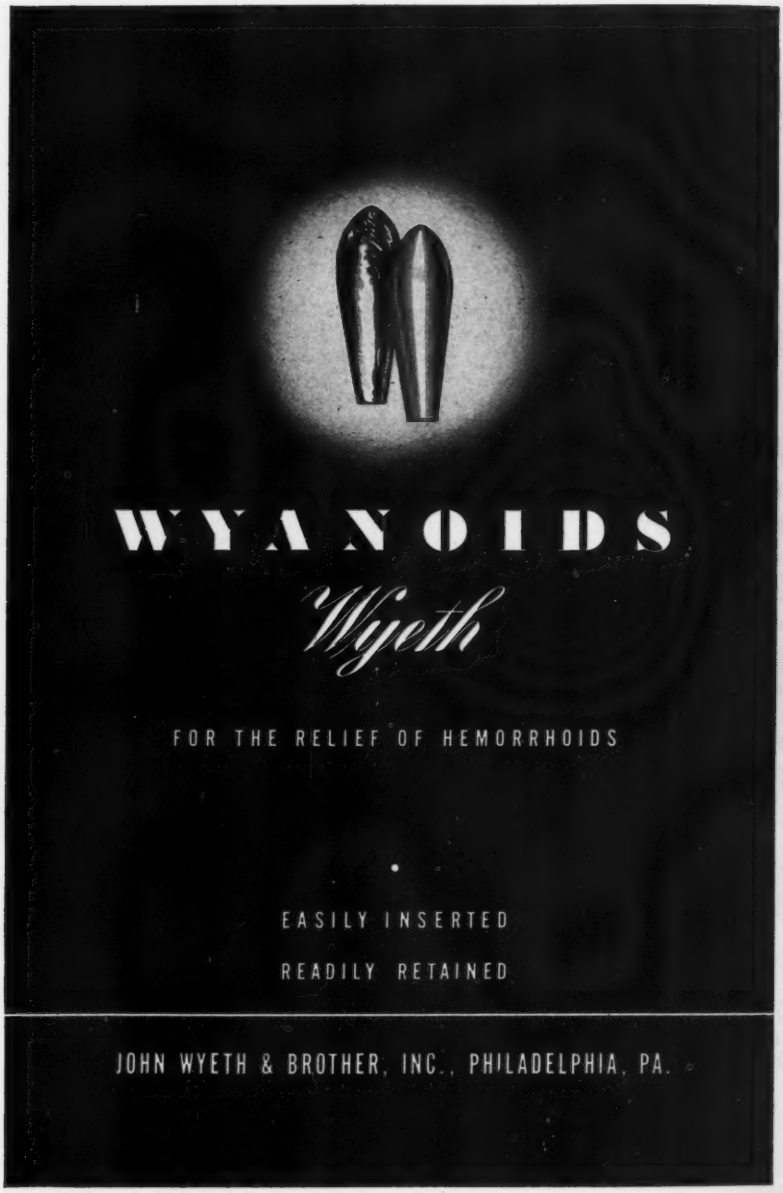
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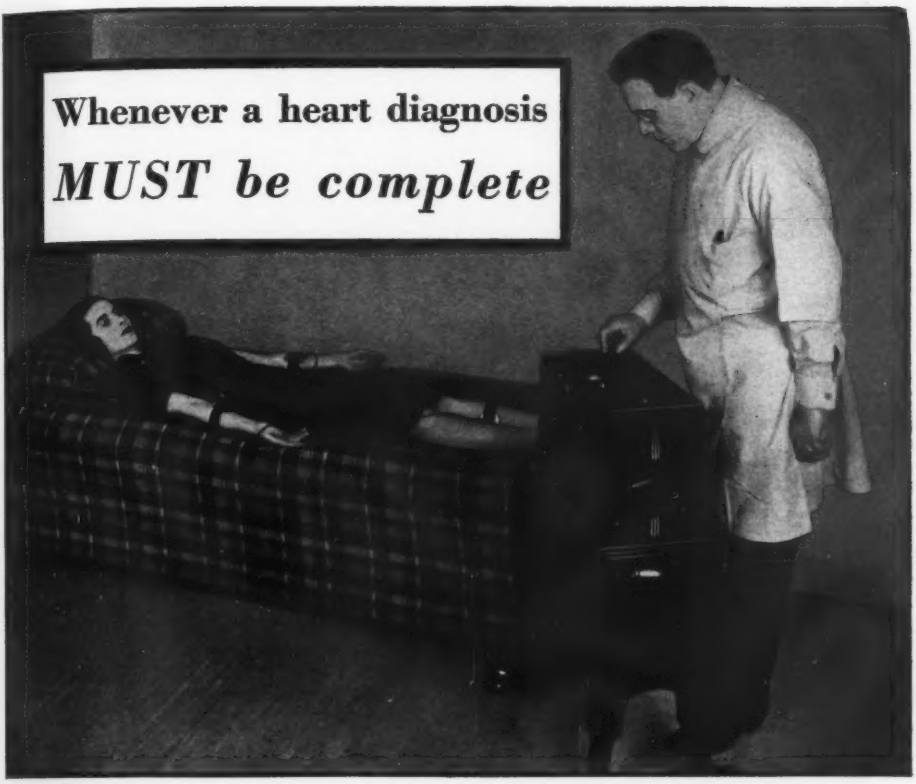

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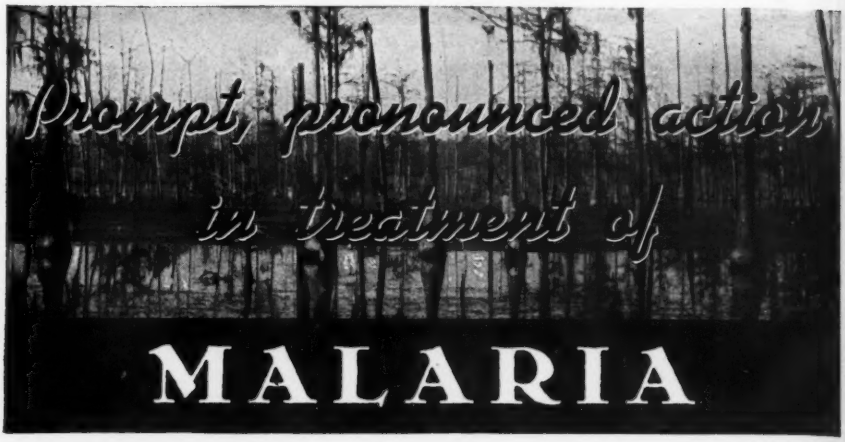

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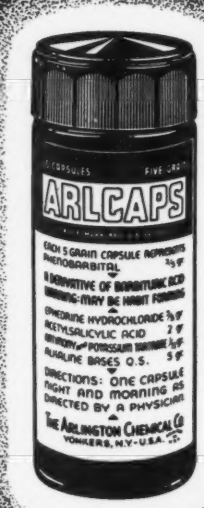

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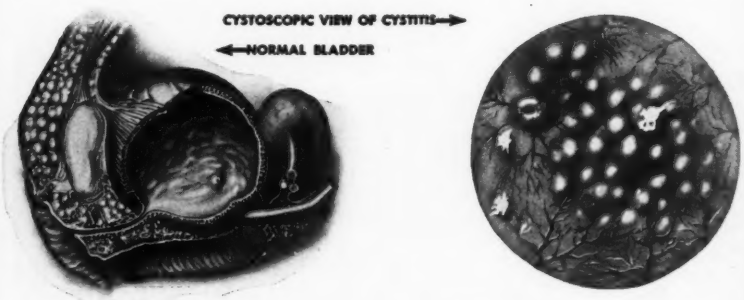

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Citrus fruits in generous quantities supply the abundance of Vitamin C required by the growing child, as well as other vitamins, mineral salts, citrates, and easily digestible sugars, in a form which appeals to all children alike.

Grapefruit, long considered a luxury, is now within the means of the greater part of our population. As a variant and supplement to other citrus fruits, grapefruit juice increases the child's intake of vitamins and minerals which are essential to the growth of straight, strong bones and sound teeth.

Once a child acquires the taste for grapefruit juice, it is relished at all times. It is a palatable, healthful beverage, and in canned form is high in all the values attributed to fresh fruit. Furthermore, canned grapefruit juice is economical, convenient to use and readily available the year around.

The Citrus Commission of the State of Florida has just issued a treatise on the subject of citrus fruits in their relation to health; a copy will be sent to any member of the medical profession upon receipt of the attached coupon.

FLORIDA CITRUS COMMISSION
STATE OF FLORIDA

Florida Citrus Commission Dept. 29-M
Lakeland, Florida

Gentlemen:
Please send me your book, CITRUS FRUITS AND HEALTH.

Name_____

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City_____ State_____

Profession_____

The statements in this advertisement are based on the following numbered references in "Citrus Fruits and Health": 8, 47, 51, 56, 59, 60.

Diarrhea in Infancy

Take It In Time

Just a day or two of light nourishment prepared from Mellin's Food as suggested below will usually avert an intestinal disturbance that might develop into a serious diarrhea if not taken in hand at the first appearance of loose stools.

Mellin's Food*. . . 4 level tablespoonfuls

Water (boiled, then cooled) . . . 16 ounces

Give one to three ounces every hour or two until the stools lessen in number and improve in character.

The mixture may then be strengthened by the gradual substitution of boiled skimmed milk for water until the quantity of skimmed milk is equal to the normal quantity of milk used in the baby's formula. Finally the fat of the milk may be gradually replaced by skimming less and less cream from the milk.

Samples sent to physicians upon request.

Directions for using Mellin's Food are left entirely to the physician.

Mellin's Food Company, Boston, Mass.

**MELLIN'S FOOD: Produced by an infusion of Wheat Flour, Wheat Bran and Malted Barley admixed with Potassium Bicarbonate — consisting essentially of Maltose, Dextrins, Proteins and Mineral Salts.*

Away from Home

★★ **Petrolagar**

Vacations mean a change of diet, water, exercise. Daily routine is altered and bowel Habit Time interrupted. This combination of circumstances tends to have a constipating effect.

Instead of quick acting harsh catharsis, the gentle softening action of Petrolagar promotes motility and encourages a regular, comfortably passed stool.

Petrolagar is miscible with liquids. It may be given orally or in an enema to assist in the restoration of a regular Habit Time of Bowel Movement.

Petrolagar . . . liquid petrolatum 65 cc. emulsified with 0.4 Gm. agar in a menstruum to make 100 cc.

Petrolagar Laboratories, Inc. • 8134 McCormick Boulevard • Chicago, Illinois

Reducing the Pellagra Death Rate

VEGEX
FOR THE B VITAMIN COMPLEX

In the American Journal of Digestive Diseases, April 1939, page 123, Dr. Frederick R. Taylor of High Point, North Carolina, gives the pellagra death rate of that State for 1923 at 224; for 1928 at 847. The high death rate of 1,015 in 1930 was brought to 327 in 1937. From 1923 to 1928 there was less of organized survey, diagnosis and treatment.

Vegex-Vitafood Dried Brewers' Yeast Aided

With some shipments in 1927, 1928, 1929 and beginning in 1930, there has been upwards of forty thousand pounds of Vegex-Vitafood Dried Brewers' Yeast, Green and Red Label, annually sent into North Carolina; widely distributed from Asheville to Winston-Salem, as well as large amounts into other Southern States.

A questionnaire sent to Southern physicians in 1937 showed that 91.1% of the large number replying use Vegex-Vitafood Dried Brewers' Yeast in successful pellagra treatment; 98% of the forty replying from North Carolina.

This dried brewers' yeast was put into the South at a price to meet the economic level of those afflicted with pellagra; with no other selling except letters to physicians and health departments and, during the last several years, advertisements in the Southern Medical Journal. Further, the best sales survey we can make is that Vegex-Vitafood Dried Brewers' Yeast has been far ahead of any other dried brewers' yeast or dried yeast and the only straight product, without the hop bitterness removed, which has been the main type used in North Carolina and other Southern States.

Current Biological Tests

Current tests show that 20 milligrams—50 International units per gram—give a higher B_1 figure than the reference standard with thiamin and that the Sherman-Bourquin test for B_2 shows 35 plus units per gram. Five per cent in the diet as the sole source of vitamin B complex continues to give good normal growth, reproduction and rearing of the litter with test animals.

Needed with Nicotinic Acid

Within the last several years nicotinic acid has been brought to the aid of pellagra relief, but now with general agreement that it cannot, alone, take the full place of dried brewers' yeast or an extract from it, like Vegex. Needed with the nicotinic acid is either dried brewers' yeast or other sources of the full P-P factor and the full B complex to do the full job.

●

Samples for clinical or professional use will be sent on request

VITAMIN FOOD CO., INC. 122 HUDSON STREET NEW YORK, N. Y. **VEGEX, INC.**

Wyeth's

SULFUR FOAM APPLICATORS

for the External Application of Sulfur

WYETH'S Sulfur Foam Applicators eliminate the objectionable messiness, smell and discomfort of most sulfur ointments and are acceptable to the patient.

Sulfur Foam is an effective prophylaxis and treatment for scabies and is gaining popularity in other cases where sulfur is indicated externally.

In Sulfur Foam Applicators, the sulfur and a bland soap are impregnated in a special wash cloth. The patient merely moistens the cloth and lathers the area to be treated. The lather dries, leaving a film of sulfur in direct contact with the area.

Wyeth's Sulfur Foam Applicators are supplied in packages of three cloths.

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SOLUBLE FERROUS IRON

● The iron in Hematinic **Plastules** is *ferrous iron*—easy to take, easy to assimilate. In the soluble, ferrous state this iron is readily available for conversion into hemoglobin.

Hematinic **Plastules** usually hasten the restoration of normal hemoglobin levels without the untoward effects of massive iron feedings.

Suggested dosage—three Hematinic **Plastules** Plain or six Hematinic **Plastules** with Liver Concentrate, daily.

℞ Hematinic **Plastules** Plain or Hematinic **Plastules** with Liver Concentrate for the treatment of secondary anemia

Available in bottles of 50's and 100's

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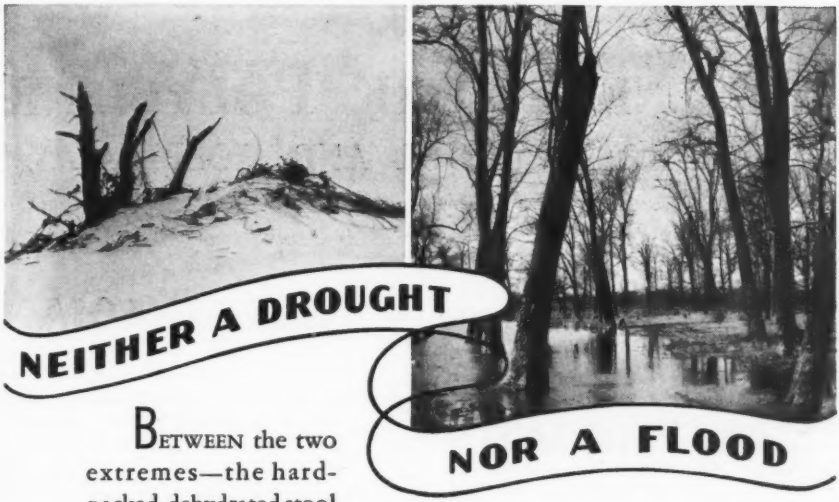

BETWEEN the two extremes—the hard-packed, dehydrated stool of constipation and the fragmented, semi-liquid feces of diarrhea—there is a norm, a normal stool characteristic of normal function.

MUCILOSE

The success of Mucilose in the therapy of constipation and spastic colitis lies in its capacity to produce a more nearly normal condition of the fecal content by controlling "water balance."

Mucilose affords valuable symptomatic relief in colitis and constipation by holding water in the feces and thus increasing responsiveness of the physiologic mechanism of peristalsis.

Mucilose offers a hemicellulose (vegetable gum) prepared by a special process from the Plantago loeflingii.

For relief of colic or spasm

CYVERINE HYDROCHLORIDE

Relaxes smooth muscle • Inhibits peristalsis
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ANESTHESIA

Regional and spinal (cadaver), with demonstrations in the clinics of caudal, spinal, nerve and field block, covering surgery in Urology, Gynecology and General Surgery. Anesthesia in general, with lectures and demonstrations.

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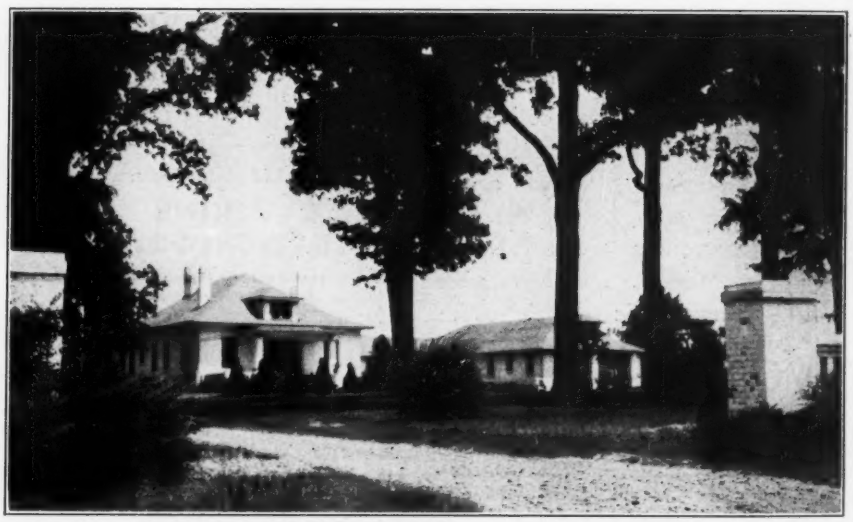

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For the Diagnosis and Treatment of Mental and Nervous Disorders

Located on the Raleigh-La Grange Road, five miles east of the city limits. Accessible to U.S. 70 (the Bristol Highway). 53½ acres of wooded land and rolling fields. Equipment new and modern, including the latest equipment for physical and hydrotherapy. Special emphasis is laid upon occupational and recreational therapy under the supervision of a trained therapist. An adequate nursing personnel gives individual attention to each patient.

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This is a private Sanatorium for the Neurological Practice of Drs. Beverley R. Tucker, Howard R. Masters and James Asa Shield.

The Tucker Sanatorium is for the treatment of nervous and endocrine diseases. There are departments of massage, medicinal exercises, hydrotherapy and physiotherapy. The Sanatorium is large and bright, surrounded by a lawn and shady walks, large verandas and has a roof garden. It is situated in the best part of Richmond and is thoroughly and modernly equipped. The nurses are specially trained in the care of nervous cases.

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A Beauty Spot on Prospect Hill

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SAN ANTONIO, TEXAS

JAMES L. ANDERSON, M.D., Medical Director

Admits patients irrespective of denomination or creed.

Ideal all year climate.—Excellent medical and nursing care.—Radiographic, Fluoroscopic and Pneumothorax service.

New, distinctive, Individual **Bungalows**, highly modern, and **Private Rooms** with baths and sleeping porches, all equipped with radio.—Beautiful grounds.

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The operating rooms and all of the front bedrooms are completely air-conditioned.

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The School of Nursing is affiliated with Johns Hopkins Hospital School of Nursing in Baltimore for a three months' course each in Pediatrics and Obstetrics.

Address: Director of Nursing Education

Laboratory and X-Ray Course

IS NOW TEN MONTHS IN DURATION

Supplemented by Six Months' Practical Work in a Hospital Laboratory, comprising 16 months in all.

COURSE INCLUDES:

Clinical Pathology
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A corps of experienced teachers plus completely equipped teaching laboratories covering 3100 square feet.

Write for new catalogue (1940)

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3514 Lucas Avenue, St. Louis, Missouri
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A Modern Ethical Sanatorium at Louisville

Founded 1904

Mental and Nervous Diseases

BEAUTIFUL AND SPACIOUS GROUNDS AFFORD OUTDOOR RELAXATION

Our **ALCOHOLIC** treatment destroys the craving, restores the appetite and sleep, and rebuilds the physical and nervous condition of the patients. Liquors withdrawn gradually; no limit on the amount necessary to prevent or relieve delirium.

MENTAL patients have every comfort that their home affords.

The **DRUG** treatment is one of gradual reduction; it relieves the constipation, restores the appetite and sleep; withdrawal pains are absent. No Hyoscine or rapid withdrawal methods used unless patient desires same.

NERVOUS patients are accepted by us for observation and diagnosis, as well as treatment.

Select Cases of SENILITY accepted. **Physiotherapy—Clinical Laboratory—X-Ray** **Consulting Physicians**

Rates and folder on request

THE STOKES HOSPITAL

Telephones Highland 2101-2102

E. W. STOKES, M.D., Medical Director, 923 Cherokee Road, Louisville, Ky.

Hoye's Sanitarium

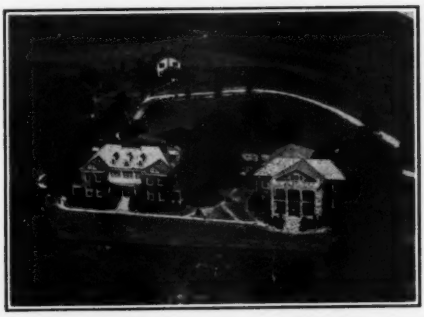
"In the Mountains of Meridian"

MERIDIAN, MISS.

Diagnosis and Treatment of Nervous and Mental Diseases, Alcoholic and Drug Addictions. Especially equipped for the Treatment of Mental Disorders. Convalescents, Elderly People and those requiring METRAZOL THERAPY given special monthly rates. Personal supervision of patients. Consulting physicians.

Dr. M. J. L. Hoye, Supt.

Formerly sixteen years Superintendent of East Mississippi State Hospital



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A modern, ethical institution, fully equipped for the diagnosis, care and treatment of nervous and mental diseases and selected addiction cases. 2,000 feet elevation. Rates reasonable. Occupational and Hydrotherapy Departments.

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Established 1890 **MILLEDGEVILLE, GA.**

For the treatment of

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Grounds 600 Acres — Buildings Brick, Fireproof — Comfortable — Convenient — Site High and Healthful

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Terms Reasonable

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For Nervous and Mental Diseases, Drug and Alcohol Addiction and Nervous Invalids Needing Rest and Recuperation

Established 1903. Strictly ethical. Location delightful summer and winter. Approved diagnostic and therapeutic methods. Seven buildings, each with separate lawns, each featuring a small separate sanitarium, affording wholesome restfulness and recreation, in doors and out doors, tactful nursing and homelike comforts.

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SMYRNA, GEORGIA
(Suburb of Atlanta)

● *For Nervous and Mental Disorders Drug and Alcohol Addictions*

Approved diagnostic and therapeutic methods. Hydrotherapy, Electrotherapy, Massage, X-Ray and Laboratory.

Special Department for General Invalids and Senile Cases at Monthly Rates.

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APPALACHIAN HALL

Asheville, North Carolina

An Institution
FOR
Rest,
Convalescence,
the diagnosis and treatment of
NERVOUS
AND
MENTAL
DISORDERS,
ALCOHOL
AND
Drug Habituation

Appalachian Hall is located in Asheville, North Carolina. Asheville justly claims an unexcelled all year round climate for health and comfort. All natural curative agents are used, such as physiotherapy, occupational therapy, outdoor sports, horseback riding, etc. Five beautiful golf courses are available to patients. Ample facilities for classification of patients. Rooms single or en suite with every comfort and convenience.

For rates and further information write
Appalachian Hall, Asheville, N. C.

WM. RAY GRIFFIN, M.D. M. A. GRIFFIN, M.D.

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ST. LUKE'S HOSPITAL

Richmond, Virginia

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The institution is situated just beyond the northern border of the city on United States Highway Number 1.

The scope of the work of the Sanatorium is limited to the diagnosis and the treatment of nervous and mental disorders and to the addictions to drugs and to alcohol. It affords also adequate facilities for rest and upbuilding under medical and nursing supervision.

The medical staff devotes its entire attention to the patients in the Sanatorium.

The institution maintains a school for trained attendants in which instruction in the care of the nervous and mentally sick is emphasized.

There are twelve separate buildings for patients, with 150 beds. Such a large group of buildings makes possible the more congenial grouping of patients. Rooms may be had single or en suite, with or without private bath. There are a few small cottages for the use of individual patients.

A comprehensive general physical and nervous examination is made of each patient. A mental examination is made when indicated. The examination is typed and a copy of it is available for the referring physician. Complete dental investigation is a part of the general survey.

A skilled teacher gives practical daily instruction to small groups in the arts and crafts. Helpful and interesting occupation in the out-of-doors is made possible for the men patients in the vegetable and flower gardens, on the truck farm, in the poultry yards, and in the dairy.

There are bowling, tennis, croquet and pool. On Sunday evening there is chapel service.

Detailed information is available for physicians.

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CITY VIEW SANITARIUM

For MENTAL and NERVOUS DISEASES and ADDICTIONS

Established in 1907

AN ENTIRELY NEW PLANT ERECTED IN 1922

Separate buildings for men and women, ideally arranged and equipped with every facility for the comfort, care, and treatment of the class of patients received.

It is upon the character of service rendered, rather than upon physical facilities that the reputation of such an institution must rest, and to give every patient the maximum of individual attention and unremitting care at all times is the basic principle of our work. An efficient organization exists in all departments. There is maintained an abundantly sufficient staff of capable nurses, divided into day and night shifts, assuring to every patient constant service through each of the twenty-four hours of the day. At midnight this service is as real as at midday.

Situated in the midst of a fifty-acre tract and surrounded by a large grove and attractive lawns.

JOHN W. STEVENS, M.D.
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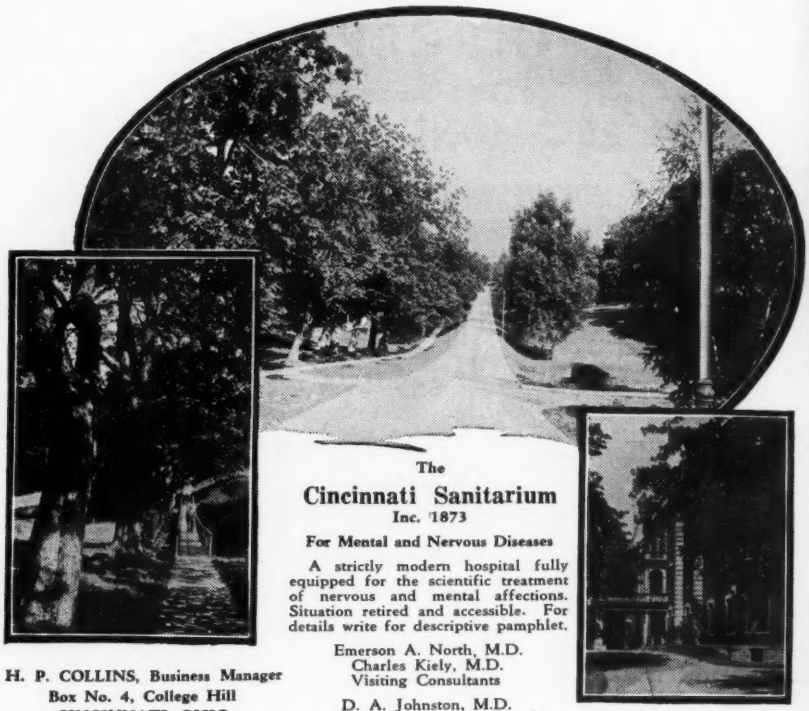
Reference: The Medical Profession of Nashville



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Cincinnati Sanitarium
Inc. 1873

For Mental and Nervous Diseases

A strictly modern hospital fully equipped for the scientific treatment of nervous and mental affections. Situation retired and accessible. For details write for descriptive pamphlet.

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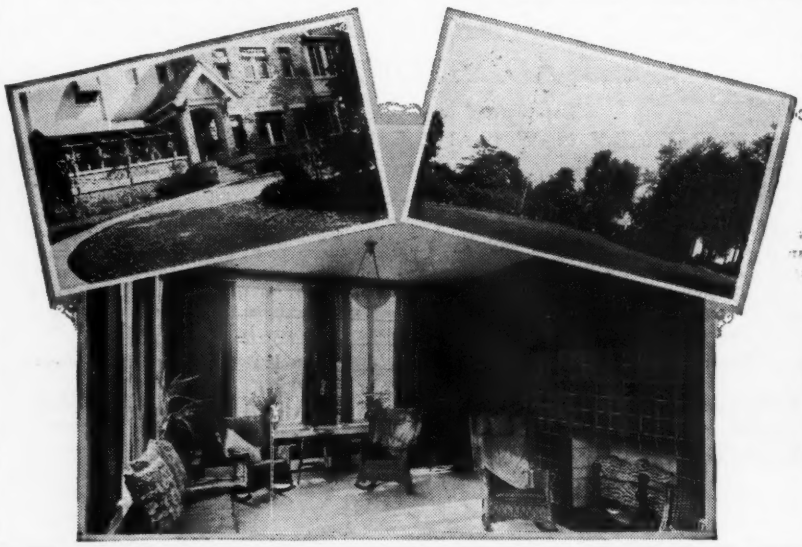
Medical Director

H. P. COLLINS, Business Manager
Box No. 4, College Hill
CINCINNATI, OHIO

"REST COTTAGE" College Hill, Cincinnati, Ohio



For purely nervous cases, nutritional errors and convalescents.

Completely equipped for hydrotherapy, massages, etc.

Cuisine to meet individual needs.

Emerson A. North, M.D.
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FOR NERVOUS AND MENTAL DISEASES AND ADDICTIONS

Metrazol and Insulin Therapy used in Selected Cases. Gradual Reduction Method used in the Treatment of Addictions

Established in 1925

Thoroughly modern in architecture and construction. Eight departments—affording proper classification of patients. All outside rooms attractively furnished. Several bathrooms and rooms with private bath on each floor. Also a spacious sun parlor in each department. Located on the crest of Higdon Hill, 1050 feet above sea level, overlooking the city, and surrounded by an expanse of beautiful woodland. Ample provision made for diversion and helpful occupation. Adequate night and day nursing service maintained.

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P. O. Box 2896, Woodlawn Station, Birmingham, Ala. **Phones 9-1151 and 9-1152**

References: Medical profession of Birmingham and Birmingham Chamber of Commerce.

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MEMPHIS **THE WALLACE SANITARIUM** **TENNESSEE**

For over thirty years in successful operation; just eight miles from the heart of the city, in a quiet suburb, occupying sixteen acres of beautiful grounds, this Sanitarium is especially equipped for the treatment of drug addiction, alcoholism, nervous, and mental disorders, the care of patients requiring metrazol and insulin therapy and is ideal for convalescents.

Gauze Always Handy

IN THIS 100 YD. DISPENSER

● When you need large cuts of gauze, you'll find this dispenser a great convenience. It contains a 100-yard roll, folded 8-ply to a 4½-inch width. Any desired length is easily drawn through the slotted opening. The dispenser is sealed, except for the slot, and the roll is kept protected inside. Two grades: Rutgers Gauze, 20 x 16 mesh; Brunswick Gauze, 20 x 12 mesh.

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SOUTHERN MEDICAL JOURNAL
JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION
PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.
Volume 33 JULY 1940 Number 7

ECLAMPSIA*

REVIEW OF THREE HUNDRED AND FIFTY CASES STRESSING THERAPY

By RICHARD TORPIN, M.D.
Augusta, Georgia
and
WILLIAM W. COPPEDGE, M.D.
East Point, Georgia

This is a clinical review of 350 cases of pregnancy with evidence of toxemia with convulsions. They were collected from a stable population of 60,000 in eastern Georgia, 60 per cent white and 40 per cent negro. The part of the study in regard to etiologic factors should be valuable because these cases represent practically all occurring in 20 years among approximately 27,000 live births, 16,000 of whom were in white women, mainly Anglo-Saxon, and 11,300 in negro women. Of the 350 cases, 183 were colored and 167 were white women. Thus, here, the ratio of incidence in the negro to that in the white population is as 11 to 7, or, eclampsia in this section is about one and one-half times as frequent in the negress as in the white woman. Eclampsia here occurs once per year among 4,320 white population and one case per year among 2,620 negro population.

In the 20 years there have been approximately 16,000 live births among white women, with an eclampsia incidence of one case per 96 live births and there have been about 11,300 negro live births with incidence of one eclamptic case per 61 live births.

Chart 1 shows the age incidence with age mortality. It is evident from this that the majority of the cases occur in the negro race from the age of 15 to 19, inclusive, and in the white from 16 to 20, inclusive. While the incidence is less in the older individuals of both races, the relative mortality is greater, the older ones evidently not being able to withstand the strain of the violent disease, especially if they already have damaged blood vessels, heart, liver, or kidneys.

In this series, eclampsia occurred about twice as frequently in the primipara as in the multipara in the colored race, but only about one and one-half times as often in the white primipara as in the white multipara. *Chart 2* shows the yearly incidence over the 20 years with the death rates per year. From this, little can be deduced as to any cyclic increase or decrease in incidence or severity, since this should show itself impartially in the two races. *Chart 3* gives the monthly incidence of all the cases and indicates mortalities over the 20-year period. Perusal of the portion for the colored patients might indicate a high incidence in April, May, June and November, but little corresponding relation to mortality.[1] However, the high rates in these four months are not present in the monthly incidence of the white patients, which should be the case if weather, heat, humidity and atmospheric pressure or seasonal and dietary changes were etiologic factors. Thirty-five white and 51 colored women had postpartum eclampsia. The degree of severity is about the same as in those cases of antepartum and intrapartum eclampsia. The therapy is essentially the same.

The first symptom, as recorded most often, appeared to be headache, which may have been present over a period of weeks. Frequently dizziness was recorded as the first symptom and occasionally visual disturbances. More common than either of these latter, but less frequent than headache, was edema of the feet, ankles and sometimes of other parts of the body. Epigastric pain ranked close to the above as the first symptom in the colored individuals, while convulsions, as the first symptom, occurred quite

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†From the Department of Obstetrics and Gynecology, University of Georgia School of Medicine, Augusta, Georgia.

frequently in the white patients, but not in the colored. Occasionally the onset was with coma, dyspnea or vomiting. Hypertension may have been present before the subjective symptoms. The rule, in this series, was hypertension with the majority above 160 systolic and above 110 diastolic. Five colored patients had a systolic blood pressure below 120, as did two white pa-

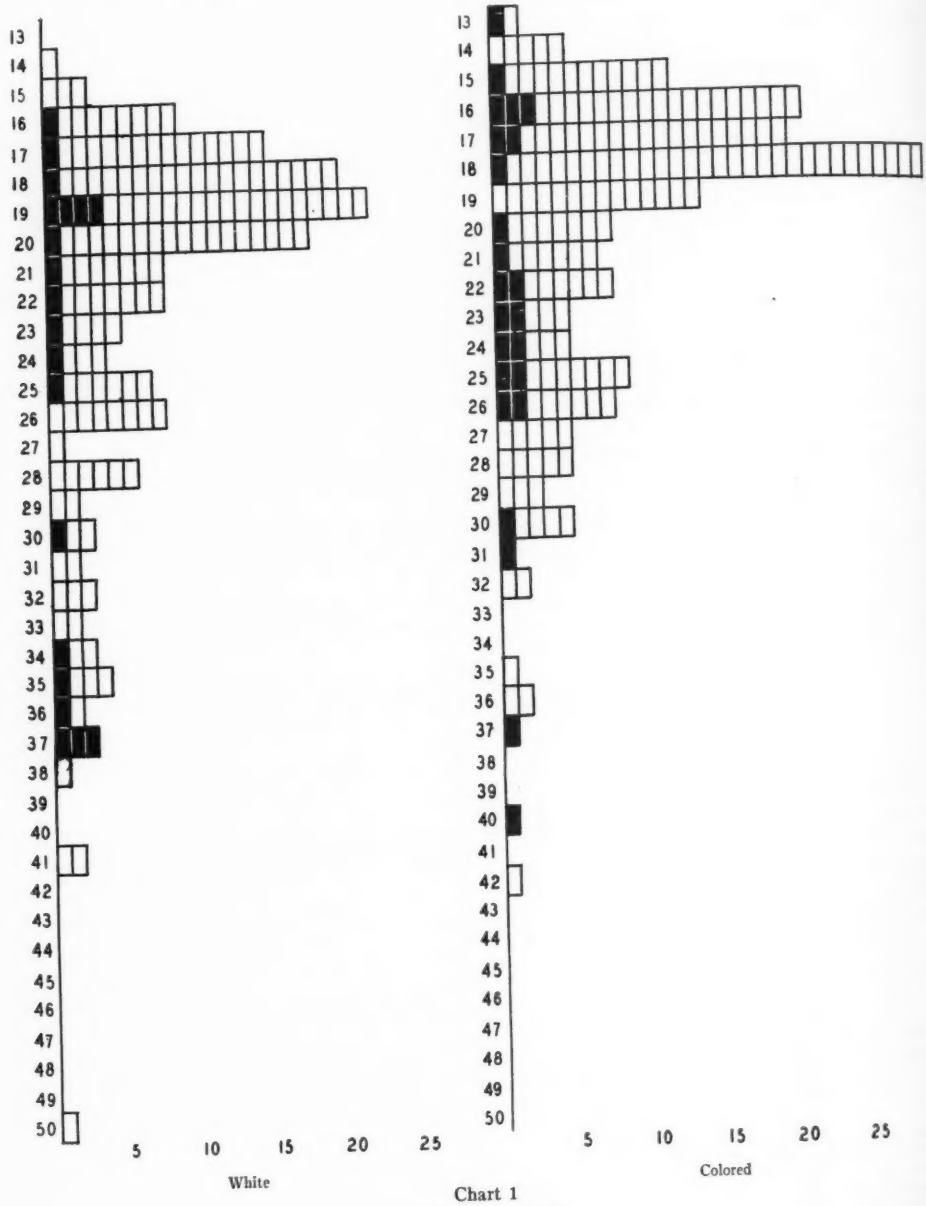


Chart 1
AGE INCIDENCE

tients also. In this group one white patient died. The low pressure may have been due to surgical shock. Extremely high systolic blood pressure (above 200) occurred in nearly one-third of the negro and in about one-fifth of the white patients. High diastolic pressures were often recorded, the highest being 180 in 1 colored and in 2 white patients, all of whom happened to recover. One negress had pressure 275/175 and recovered; another with 230/170 died; one with 244/186 recovered. White women with 270/170; 220/180; 240/180 all recovered.

Chart 4 gives in graphic form the number of patients of each race with systolic and diastolic pressures of various degrees and the accompanying mortalities.

The majority of patients had temperatures of 100-102 degrees. Higher temperatures seemed to carry higher mortality, as seen in *Chart 5*. The pulse rate (*Chart 6*) in both races, in the great majority, was 100-120. Higher pulse rates, like higher temperatures, bore a higher mortality.

Chart 7 reveals the amount of albumin in the urine in the recorded cases. Nearly one-half of the patients died in anuria, or before a record of this finding was made; consequently, the true picture is not shown. However, it is to be noted that no death occurred in the few cases where no albumin or only a trace was found.

Edema was recorded as present in 179 of the colored and 120 of the white patients. A record of no edema was made in 12 colored and in 3 white patients. There was no record of the presence of edema in the remainder of cases. Two of the fifteen without edema died. One white patient who died had little edema, but at autopsy 2,000 c. c. of clear fluid was found in the peritoneal cavity. Coma intervened between convulsions in about two-thirds of the cases, more often, apparently, in the colored than in the white women. In only 3 or 4 of each race were the patients mentally

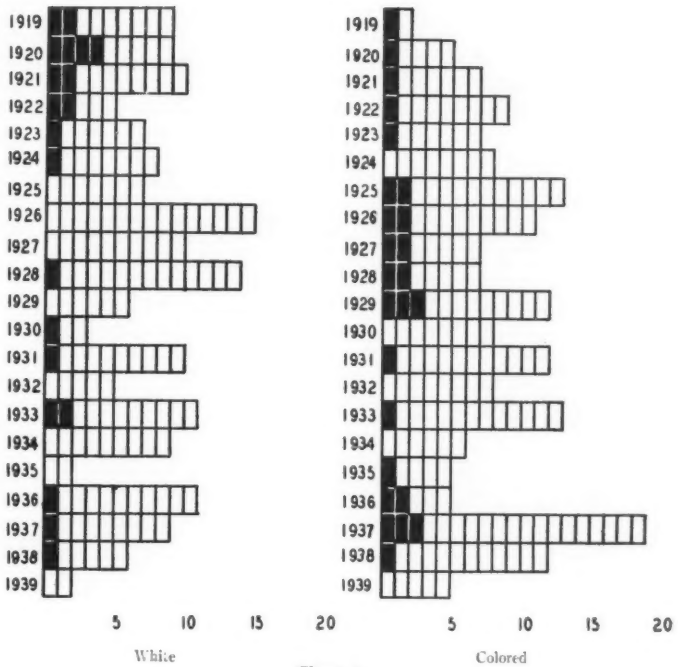


Chart 2
YEARLY INCIDENCE

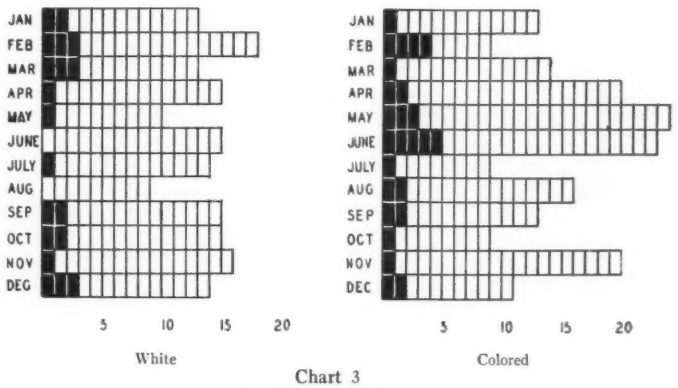
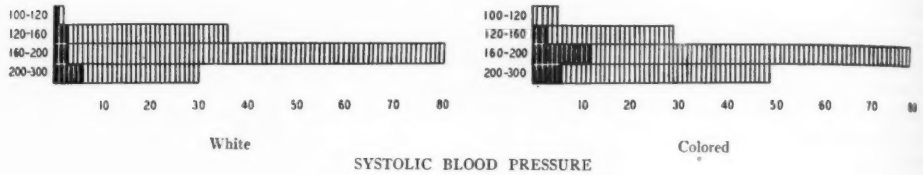


Chart 3
MONTHLY INCIDENCE

clear between convulsions and none of these died.

In regard to previous eclampsia in the same patient, five white and seven negro women had a second attack. One white patient had the disease 3 times. While this is a relatively small number of recurrences, it was frequently found that patients with eclampsia had severe pre-eclampsia or toxemia with one or more previous pregnancies. There were also seen patients who, with previous pregnancies had had eclampsia, who subsequently had severe toxemia or pre-eclampsia with later pregnancies. However, this was not at all constant, as there were seen instances of normal pregnancy occurring both before and after eclampsia pregnancies.

Eden's[2] classification is used in grouping the cases as to mild or severe types. That is, severe cases have two or more of the following symptoms or findings: (1) temperature above 103° F.; (2) pulse rate over 120 per minute; (3) blood pressure of 200 mm. of mercury or over; (4) absence of edema; (5) urine which solidifies on boiling; (6) persistent coma; (7) more than 10 convulsions. In the white patients there were 64 severe and 96 mild cases, and among



SYSTOLIC BLOOD PRESSURE

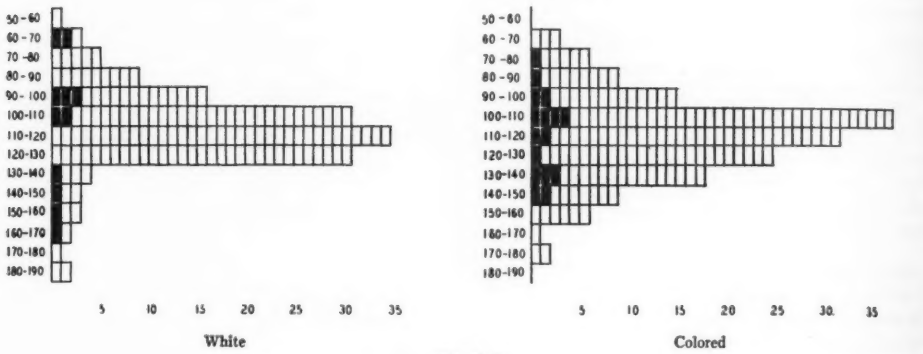


Chart 4
DIASTOLIC BLOOD PRESSURE

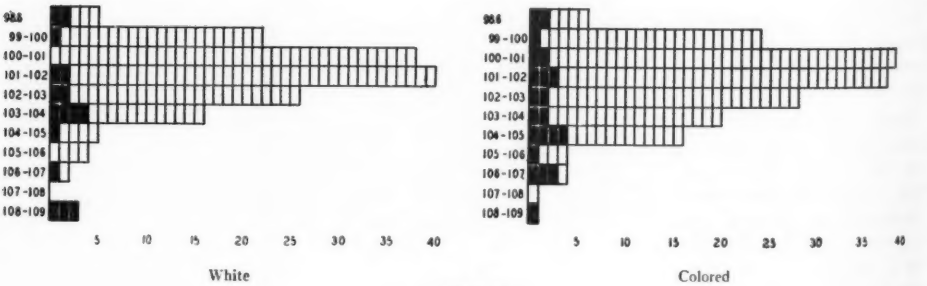


Chart 5
TEMPERATURE

the negro patients 65 severe and 102 mild, giving a total mild of 198 and a total severe of 129. It is interesting to note that about 13/20 of our series were mild, while in Baltimore in 205 cases reported by Peckham only about one-half were mild. He, however, used his modified Eden classification which increases the number of mild cases in any series.

Adequate prenatal care certainly reduces the incidence of eclampsia. In this series the disease, in those patients who had received prenatal care, was usually milder, with the exception of a very few acute fulminating cases. Only two white patients attending the prenatal clinic had severe eclampsia and succumbed. These were some private cases about which we were unable to check. Three colored patients who died attended the prenatal clinic. One of these had adequate care with negative urine and systolic blood pressure of 130 mm. of mercury two weeks before onset of the disease. There were 73 primigravida and 55 multigravida in the white cases. No history was obtained as to gravida in the remaining 32. Of the colored patients, 87 were primigravida, 44 multigravida, and 36 were not recorded.

THERAPY

With the collaboration of Dr. A. P. Briggs, Associate Professor of Biochemistry and Medicine, and with Dr. Perry Volpitto, Professor of Anesthesiology, a principle of therapy has been developed based upon physiologic and pharmacologic fundamentals as follows. The evidence points to the concept that eclamptic patients are suffering from some form of toxemia. Like the toxemia of infectious diseases, it has a great tendency to produce the shock syndrome in all varying degrees. It also has a tendency to upset the water balance. The convulsions seem to be due to some sort of edema of the brain.* While eclampsia is peculiar to pregnancy or the puerperium, the pregnancy in the acute attack seems to be irrelevant and experience has shown that it is safer to ignore it at this time than to force labor by any operative procedure. The toxemia

*"Some light on the problem may be obtained by examination of other similar symptom complexes which are also associated with cerebral edema. In various types of anoxia, cerebral edema develops because of increased capillary permeability. And the stimulation of brain centers in anoxia depends on the rate of development as well as the extent. So a cerebral edema of small magnitude but developing abruptly might cause violent symptoms. Such a situation not infrequently occurs in acute nephritis where convulsions are associated with only slight nonpitting edema.

"That an abrupt disturbance to the water balance does occur with convulsions in eclampsia is indicated by the work of Dieckmann, who observed a decrease in blood volume and an increase in blood protein to occur with attacks. These findings indicate a change in capillary permeability with forcing out of plasma fluid into the previously well-filled extracellular spaces." Briggs, A. P.; and Torpin, Richard: Amer. Jour. Obst. & Gyn., 38:960, 1938.

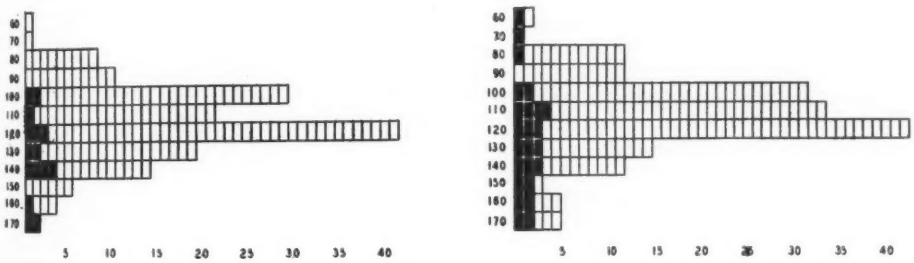


Chart 6
PULSE RATE

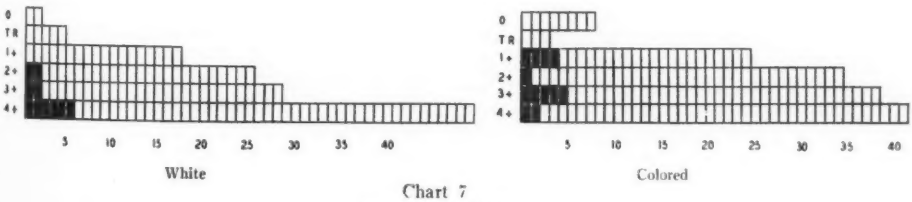


Chart 7
URINE CONTENT

of eclampsia and the conditions caused by it apparently injure the liver and the kidney by necrosis, the lungs by edema and by aspiration of foreign material, the brain by edema and the fetus by anoxemia, the heart by strain and by improper nutrition, as well as by possible direct action of the toxin. Inasmuch as there is no specific therapy, the treatment developed aims at combating all of the deleterious effects noted: (a) cessation of the convulsive seizures; (b) prevention of additional damage to any organ; (c) elimination of the toxins; (d) promotion of absolute rest; and (e) surgical shock therapy when indicated.

Routinely, the management used is as follows: as soon as the diagnosis is confirmed (blood pressure, urinary contents, and so on, ascertained) magnesium sulphate, 20 c. c. of a 10 per cent solution, is administered intravenously, slowly and with knowledge that toxic symptoms may be manifested.[3,4] If the patient is conscious during intravenous administration of the magnesium sulphate solution, she usually says that she feels warm, most often in the pelvic organs or in the throat. This is a signal to slow the injection until the feeling disappears. Stroganoff advises that 10 c. c. of sterile 5 per cent calcium chloride solution be at hand to counteract any serious toxic manifestations of the magnesium sulphate solution. Calcium gluconate as a substitute for calcium chloride is recommended as being less necrosing if accidentally injected outside of the vein. If the patient is not in coma, she may be given by mouth one and one-half ounces of magnesium sulphate in addition to the intravenous administration. Usually the magnesium sulphate reduces the blood pressure to 160 systolic, or lower, and the convulsions cease. The magnesium sulphate may be repeated intravenously every hour as long as the systolic blood pressure is 160 or more. Although seldom required, 20 grams in 24 hours may be given thus. One patient over a period of 2 weeks persisted in hypertension and received 70 grams intravenously without ill effects and went home with blood pressure 120/70. Both mother and child recovered.

If the convulsions continue and are of short duration and mild type, paraldehyde, 4-6 drams, is given rectally and repeated as necessary. However, if the convulsions are violent and prolonged, death may intervene from anoxia before the action of paraldehyde rectally takes effect. Inasmuch as a large per cent of eclamptics die in a prolonged convulsion, these must be controlled by the most certain means known, which is immediate intravenous administration of one of the soluble barbiturates, preferably one of the longer acting ones such as sodium phenobarbital or sodium iso-amylethyl barbiturate. The amount to be given is governed by each individual case, in other words, enough of the barbiturate should be given to control the convulsions. Sodium phenobarbital may be the better choice inasmuch as it does not depend entirely on a well-functioning liver for detoxification. Only in case of violent prolonged convulsions is sodium phenobarbital given, and when they are controlled it is not repeated.

The other sedatives, besides paraldehyde, are known occasionally to damage some of the various organs mentioned or to reduce the chances for the survival of the fetus, to wit: the shorter acting barbiturates, pentobarbital, n-methyl-c-c-cyclo-hexamyl-methyl barbituric acid, sodium ethylthiobarbiturate and sodium iso-amylethyl barbiturate, are detoxified by the liver. Morphine[5] increases the intracranial pressure and may reduce the maternal respiratory rate, thereby increasing the anoxemia to the mother and consequently to the fetus. Valuable as it may be in certain conditions, morphine probably never should be used in eclampsia. Probably the best circulatory support is dextrose solution and, as in all other toxemias, enough fluid in the vessels to promote adequate circulation has proven by experience to be indicated. Consequently, even if there is edema, the full daily requirement of fluid with dextrose is administered. This, if the patient is in coma, is at least 3,500 c. c. of 5 per cent dextrose in distilled water intravenously. Used in the last 30 or 40 cases, there has been no instance of anuria resistant to salt-free fluids in these quantities and there has been absence of cardiac failure or edema of the lungs.[6,7,8]

Ware and Noblin[9] recommend the routine use of digitalis. However, cardiologists are of the opinion that digitalis is not indicated in any case unless there is actual or threatened decompensation. No salt is allowed because the sodium ion, together with hypoproteinemia of pregnancy, leads to increased water retention. M. B. Strauss,[6] K. DeSnoo[7] and M. E. Davis[8] all are in favor of limiting sodium chloride in toxemias of pregnancy. Adequate salt-free diet with iron and vitamins is recommended. Restriction to milk is not advised because of milk's high salt content. As in any acutely ill patient, rest is essential and should be the prime con-

sideration of good nursing care. In a darkened and quiet room the patient should be subjected to as little manipulation and during a convulsion to as little restraint as possible to prevent injury. A wooden mouth gag should be handy to avoid tongue biting. To obviate aspiration of stomach contents when the patient is in coma the foot of the bed may be elevated, or the patient kept on her side, and we often gently insert a nasal suction tube into the stomach for continuous aspiration.

To counteract anoxemia, oxygen should be administered for the mother's as well as for the baby's welfare. If there is anemia, repeated blood transfusions are indicated. If the patient is one of the two-thirds or more who have the attack prior to delivery, her condition is allowed to improve or become stationary. She is then subjected to induction of labor, accomplished, as a rule, by rupture of membranes, if at term or by bougie or a bag insertion if premature. An x-ray film of her inlet[10] with the fetal head is made and if the relationship is satisfactory she is allowed to deliver spontaneously, or, if the head stops at the perineum or in the mid-pelvis for a period of time longer than two hours after full dilatation of the cervix, the fetus is then delivered with the use of forceps with cyclopropane anesthesia. Ordinarily labor is rapid and without much apparent deleterious effect upon the mother. Very little care in regard to the fetus pays enormous dividends in reducing the stillbirth rate: first, by prevention of threatened maternal and consequently fetal anoxemia by judicious administration of oxygen to the mother; and second, by proper resuscitation of the fetus which includes keeping the baby warm, aspiration of mucus, amniotic fluid and possibly meconium from the pharynx, larynx and trachea, and gentle insufflation of the baby's lungs through a tracheal catheter, if necessary; third, by refraining from use of drugs and anesthetics which depress the respiratory movements of the fetus *in utero*. Rosenfeld and Snyder[11] have shown that these include practically all sedatives and anesthetics except cyclopropane and nitrous oxide anesthesia. Because cyclopropane is used with high oxygen content it becomes the anesthetic of choice in delivering in eclampsia, benefiting both mother and child.

Induction of labor by catheter insertion was performed in 25 per cent of the 260 antepartum cases. The incidence of forceps deliveries was recorded as slightly more than 11 per cent. Version and extraction were performed 12 times. Only one cesarean section was done.

RESULTS OF TREATMENT

The deaths among the 183 negro patients were 25, a rate of 13.6 per cent. Of the 167 white patients, 20 died, giving a mortality rate of 11.9 per cent. The combined mortality was 12.8 per cent and the stillbirth rate, among the 200 recorded, was 33 per cent in the colored and 29 per cent in the white patients. During the time of the first half of this series the principal reliance for control of convulsions was placed upon veratum veride, and in the second half upon magnesium sulphate. Although for the first few years of its use magnesium sulphate was given in smaller doses and intramuscularly, the mortality of all cases in which it was used is slightly less than 9 per cent, a reduction of 35 per cent from the general mortality. Too much dependence upon these figures cannot be made in view of Peckham's[12] statement that his mortality rate over the same period fell equally, without any change in the management. Nevertheless, almost all clinics report satisfaction with magnesium sulphate in apparently reducing the death rate. In 1934, McCord,[13] at Atlanta, reported 115 cases with 6 deaths, a mortality rate of 5.2 per cent. He used nothing but magnesium sulphate and dextrose solutions.

SUMMARY

(1) Three hundred and fifty cases of eclampsia have been reviewed. The incidence is 50 per cent greater in the negro than in the white women. The half decade, 15-20 years, included the ages of the large majority of either race. It is more frequent in the primipara. In this study there was practically no evidence of cyclic variation in incidence over a period of 20 years and practically none in regard to the monthly incidence. Consequently, a relation in occurrence of the disease, in regard to weather, heat, humidity and atmospheric changes was not evident.

(2) The symptoms in the series of 350 cases of eclampsia were analyzed. There was a higher mortality in the negro than in the white patients.

(3) A five-point treatment in eclampsia is outlined: (1) Two grams of magnesium sulphate intravenously in sterile 10 per cent solution every hour as long as the systolic blood pressure is 160 or more. Twenty grams in 24 hours may be necessary. Convulsions must be stopped, if mild, by paraldehyde in 4-6 dram doses rec-

tally; if severe, sodium phenobarbital solution is given intravenously only until control. (2) Adequate salt-free diet is given. (3) Thirty-five hundred c. c. of 5 per cent dextrose in sterile distilled water is given intravenously daily when the patient is in coma. Administration of oxygen and blood is used when indicated. (4) Absolute rest is required with the foot of the bed elevated and duodenal nasal tube with constant suction when the patient is comatose to prevent aspiration pneumonia. (5) When the condition improves or becomes stationary, induction of labor by rupture of membranes, if at term, or by catheter or bag insertion if earlier, should be done.

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DISCUSSION (*Abstract*)

Dr. Earl Conway Smith, New Orleans, La.—Time permits only a brief discussion of this excellent presentation on eclampsia from the point of view of prophylaxis and management.

Adequate prenatal care should include:

(a) a good history and physical examination;

(b) routine care with maintenance of good health;

(c) antenatal examinations; bimonthly to the eighth month, weekly thereafter, and more often, if necessary; and

(d) explanation to the patient of the commonest abnormal symptoms and signs so that she may report early on their occurrence.

Early recognition of a developing toxemia is important. The symptoms are: headache, nausea, vomiting, constipation, salivation, jaundice, visual disturbances, edema, suppression of urine. Any one of these may develop several weeks before the onset of convulsive seizures.

Pregnancy is normally characterizd by a positive water balance. This retention of water is most marked in the last half of gestation. A rapid gain in weight may be one of the earliest signs of impending toxemia which is indicative of fluid and sodium chloride retention. A woman gains normally about twenty-two pounds during pregnancy, while a toxic woman may gain forty to fifty pounds. When this weight gain is six to ten pounds in seven to fourteen days, we must assume there is abnormal water storage and should institute prompt measures to favor elimination.

When a toxemia is developing, there is almost invariably a distinct rise in both systolic and diastolic blood pressures several weeks before albumin appears in the urine. This may, indeed, be the first sign to develop. A patient whose normal average pressure is 100/60 and who exhibits a rise to 120/70, and one whose normal average pressure is 120/70 and who exhibits a rise to 160/90, are indeed candidates for toxemia. A diminishing pulse pressure, therefore, may indicate impending cardiovascular collapse. We must not overlook the occasional case, however, that presents toxic symptoms with apparently normal blood pressure.

Frequent chemical and microscopic examinations of 24-hour specimens of urine may reveal very definite findings of impending toxemia. In addition to the testing of urine for the presence and amount of albumin, the measured daily output of urine with specific gravity, compared to the measured intake of fluids, is significant. The daily output of urine in a normal case is about 1,500 c. c., with a specific gravity of 1.010 to 1.025. If the output is decreased to 800 c. c. or less, and if the specific gravity is less than 1.010, it is indicative of impending toxemia. I would like to state here that most of the popular renal function tests, urea clearance, phenolsulfonephthalein, are not reliable in eclampsia, and are of value only when there is concomitant renal disease.

The lipid amino nitrogen shows a significant elevation in the whole blood of eclamptics, in 25 per cent of cases, which parallels the severity of the toxemia (Hellman, *et al.*).

Marked elevation of serum anterior pituitary-like hormones about the fifth, sixth, seventh months, precedes clinical signs four to six weeks (Smith and Smith).

Termination of gestation in eclampsia is indicated when there is:

(a) failure of patient to respond to treatment;

(b) development of toxic symptoms;

(c) cardiovascular embarrassment; or

(d) persistent oliguria or anuria.

If the baby is viable, at or near term, the pregnancy should be interrupted. When viability is questionable, conservative treatment is carried out until viability is reached, if possible. The simpler the method of termination, the better. Usually, simple rupture of membranes will suffice at or near term. At times, a suitable adjunct is posterior pituitary extract by hypodermic. In some cases it is necessary to insert a hydrostatic bag in the cervix to initiate contractions. In any event, one should be sure that no cephalo-pelvic disproportion exists.

In convulsive toxemia an accurate measure of the total fluid intake and total urinary output is essential. The measure of urinary output can be facilitated by use of a retention catheter inserted in the bladder. To promote diuresis, I, as well as others, have conclusively demonstrated that 500 to 1,000 c. c. of 20 per cent glucose solution given two or three times daily, intravenously, to edematous patients, and 1,000 c. c. of 5 to 10 per cent glucose solution two or three times daily in those cases that need fluids will promote adequate diuresis, or about 30 c. c. of urine per hour. Smaller amounts of 30 to 50 per cent glucose solution are indicated when edema is marked, or when there is evi-

dence of circulatory embarrassment. Also, limitation of sodium chloride, free purgation using magnesium sulphate, and the administration of 4 to 8 grams of ammonium or potassium nitrate daily in divided doses, will further promote diuresis and establishment of water balance.

Cesarean section should rarely be performed in the presence of convulsive toxemia unless the specific indications for section are present, and even then it should not be performed until the acute stage has been controlled by proper medical therapy. I believe that, given an elderly primipara with a long, thick, uneffaced cervix, low abdominal section is indicated. There are advocates of section in all primipara following the acute stage, but it must be remembered that statistics will show a general maternal mortality rate almost as high as forcible delivery from the vaginal route. If the patient falls into a coma without convulsions, cesarean section seldom saves the mother, but it should be done in the interest of the baby. When and if section is decided upon, it should be performed in suitable environment by trained personnel, and under local anesthesia.

Dr. Cecil E. Warde, Memphis, Tenn.—This paper shows the trend toward conservatism, and persistent treatment of preeclamptic toxemia.

As Dr. Torpin has brought out, the preeclamptic patient first shows a marked weight gain, which is almost invariably the first sign of true preeclamptic toxemia. Most of these women, if the weight gain is controlled principally by water restriction and sodium chloride elimination and starvation and magnesium sulphate, will regain their balance and go ahead.

But there is a still more important side to preeclamptic toxemia. The patient who has arrived at the middle of her pregnancy in good health, is lean and strong and vigorous and well tanned, will not be likely to develop preeclamptic toxemia.

The introduction of magnesium sulphate through the duodenal tube during the convulsive state is rather important.

PROGRESS IN SYPHILIS CONTROL IN THE SOUTHERN STATES*

By J. R. HELLER, JR., M.D.†
New Orleans, Louisiana

This progress report in syphilis control in the Southern states was derived mainly from tabulation of data from questionnaires obtained by the U. S. Public Health Service from state health departments and from monthly morbidity and other miscellaneous reports. The material in this paper is intended to serve as a basis for more adequate analysis of what is to be done in the future as well as to indicate progress during the last four years.

Impetus was given syphilis control in the Southern states when funds became available for cooperative health work with the states under Title VI of the Social Security Act. Additional momentum was imparted by the conference on Venereal Disease Control in Washington, D. C., in December, 1936, where something concrete and tangible was offered to the states in the clinical and administrative management of venereally infected individuals. In every state programs were developed which embraced many of the essential elements of venereal disease control. Attention was directed toward training clinicians and administrators, improving diagnostic facilities, extending and improving treatment service, projecting educational programs, improving case holding and case finding activities and obtaining increased appropriations from state and local sources. A favorable public sentiment has been established gradually and the general response has been gratifying.

In May, 1938, the LaFollette-Bulwinkle Bill, which was an amendment of the Venereal Disease Act of July 9, 1918, was passed by Congress, together with an accompanying appropriation of $3,000,000 to carry out the provisions of the Act for the fiscal year, 1939. With these additional funds states were enabled to extend, more completely, syphilis control programs. In many instances activities directed toward syphilis control were an entering wedge in establishing local health service. For the fiscal year 1940, five million dollars were appropriated for venereal disease.

The sixteen Southern states and the District of Columbia, commonly referred to as "The South," have a total population of 37,619,253.[1] There are 46,251 physicians in this area, Texas leading with 6,795 and South Carolina trailing with 1,354. There is an average of 813 persons per physician in the South. The District of Columbia has the lowest, 227, and Mississippi the highest with 1,344 per doctor. The average for the United States is 724 persons per physician.[2] The average per capita annual income of the South is $315, Mississippi having the lowest with $148 and the District of Columbia the highest with $694. The average per capita annual income of the United States is $428.[3]

In the South the estimated incidence of syphilis based on twenty-two surveys in representative areas, both urban and rural, indicates that, although only 30 per cent of the population of this country resides in the sixteen Southern states and the District of Columbia, 65 per cent

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†Passed Assistant Surgeon, United States Public Health Service.

of all individuals in the United States who acquire syphilis each year are in this area.[4] This estimate has served to focus attention on this section of the nation as a reservoir of syphilis. Ignorance, poverty, superstition and inadequate medical service in many rural areas, together with a large negro population, in which the prevalence of syphilis is much greater than in the white race, are factors which tend to sustain the high incidence of this disease. This situation is not an enviable one, but it stands as a challenge to change or amend the factors involved.

Progress in syphilis control can be measured best, perhaps, by a comparison of facilities and activities existing before the availability of Social Security and Federal venereal disease funds, during the fiscal year 1935, and those observed to June 30, 1939, a four-year period. Since the venereal disease control funds did not become available until the beginning of the fiscal year 1939, marked progress has been noted during the last twelve months.

Table 1

CASES OF SYPHILIS REPORTED TO STATE HEALTH DEPARTMENTS DURING THE FISCAL YEARS 1935 AND 1939, THE CASE RATES PER 1,000 POPULATION, AND THE PERCENTAGE INCREASE IN THE NUMBER OF CASES AND IN THE CASE RATE.

17 SOUTHERN STATES

	1935		1939		Percentage Inc.	
	Cases of Syphilis	Rate per 1,000 Population	Cases of Syphilis	Rate per 1,000 Population	In Number of Cases	In Rate per 1,000 Population
Alabama	4,692	1.67	20,957	7.16	346.7	328.7
Arkansas	4,751	2.40	10,296	4.96	116.7	106.7
Dist.of Col.	1,839	3.28	6,278	9.87	241.4	200.9
Florida	5,438	3.43	13,559	7.98	149.3	132.7
Georgia	9,625	3.20	26,741	8.59	177.8	168.4
Kentucky	2,652	.94	10,519	3.55	296.6	277.7
Louisiana	2,150	1.02	9,530	4.44	343.2	335.3
Maryland	9,291	5.58	12,930	7.67	39.2	37.5
Mississippi	13,290	6.62	27,545	13.50	107.3	103.9
Missouri	6,404	1.66	11,229	2.79	75.3	68.1
N. Carolina	14,210	4.21	27,137	7.69	91.0	82.7
Oklahoma	1,995	.80	6,327	2.46	217.1	207.5
S. Carolina	3,190	1.75	10,812	5.71	238.9	226.3
Tennessee	6,490	2.33	12,920	4.42	99.2	89.6
Texas	5,692	.94	31,197	5.01	448.1	433.0
Virginia	4,945	1.90	20,111	7.33	306.7	285.8
West Virginia	3,525	1.96	4,679	2.46	32.7	25.5
Total	100,179	2.31	262,767	5.83	162.3	152.3

Reporting of syphilis by private physicians and hospitals has increased by 162.3 per cent during the past four years. More active interest on the part of private practitioners, better facilities to properly "follow through" a case once it is reported, and better understanding generally of the aims of syphilis control programs are chiefly responsible for this increase. Texas has the greatest increase with 448 per cent and West Virginia the lowest with 32.7 per cent. In several states where syphilis control programs have been in operation for some time, pronounced increases probably could not be expected. Improved syphilis morbidity reporting cards have been adopted by practically all the states. *Table 1* presents the reporting of syphilis by states.

As of June 30, 1939, every Southern state had a separate division or subdivision of venereal disease control, whereas only four of the seventeen states had an administrative unit of venereal disease control in 1935. Twelve have full-time venereal disease control officers in 1939 as compared with two in 1935. Many have more than one venereal disease control officer and, in addition in June, 1939, thirteen had Public Health Service officers assigned them as con-

Table 2

STATE HEALTH DEPARTMENTS WITH SEPARATE DIVISIONS OR SUBDIVISIONS AND FULL-TIME OFFICERS FOR THE CONTROL OF VENEREAL DISEASES AS OF JUNE 30, 1935, AND JUNE 30, 1939.

STATE	Subdivision or Separate Division		Full-Time Officer	
	1935	1939	1935	1939
Alabama	no	yes	no	yes
Arkansas	no	yes	no	no
District of Columbia	yes	yes	no	no
Florida	no	yes	no	yes
Georgia	yes	yes	yes	yes
Kentucky	yes	yes	no	yes
Louisiana	no	yes	no	yes
Maryland	no	yes	no	no
Mississippi	no	yes	no	yes
Missouri	no	yes	no	no
North Carolina	no	yes	no	yes
Oklahoma	no	yes	no	yes
South Carolina	no	yes	no	yes
Tennessee	no	yes	no	no
Texas	no	yes	no	yes
Virginia	no	yes	no	yes
West Virginia	yes	yes	yes	yes
Total departments with divisions or officers	4	17	2	12
Per cent increase	32.5		500.0	

sultants in their venereal disease control programs. During the present fiscal year it is expected that all states will have full-time trained medical officers to administer the program. *Table 2* presents these administrative data in detail.

Since treatment is still considered the sheet anchor in the control of syphilis, availability of treatment for the individual unable to pay any or part of the regular fee is of distinct value in appraising a syphilis control program. There has been an increase in the number of hospitals and dispensaries which offer treatment for the venereal diseases of from 285 in 1934 to 1,351 in 1939, or an increase of 374 per cent. North Carolina had the greatest increase during this period and the District of Columbia the smallest. Only one state, South Carolina, had no clinics for the treatment of syphilis in 1934 as reported officially to the U. S. Public Health Service. Two, North Carolina and Georgia, have mobile treatment units operating in circumscribed rural areas and during the fiscal year, 1940, four more, South Carolina, Alabama, Missouri and Arkansas, will operate similar mobile units. *Table 3* presents the increase in treatment clinics by states.

Free drugs are distributed for the treatment of syphilis of indigent cases by all the Southern states as of June 30, 1939. In 1935, only nine states furnished drugs on this basis. In 1939 drugs are furnished irrespective of economic status, or to all, in four states, whereas in 1935, only one, Maryland, observed this practice. Private practitioners of medicine are treating many more indigent or medically indigent patients as a result of the free distribution of drugs. The recommendation adopted by the state and territorial health officers concerning the free distribution of drugs to all has not been generally adopted. These data are presented in detail in *Table 4*.

No Southern states required premarital examination for syphilis as of 1935, but in 1939 legislation in four states provides for compulsory examination prior to marriage, with this examination including a serodiagnostic test for syphilis from a reputable and approved laboratory. Similarly, two states in 1939 have compulsory legislation providing for examination of pregnant women for syphilis, whereas no such legislation was in effect in 1935. Laws for both premarital and prenatal examinations for syphilis have been considered in the majority of the

Table 3

NUMBER AND PER CENT INCREASE BY STATE OF HOSPITALS AND DISPENSARIES FOR THE TREATMENT OF VENEREAL DISEASES AS OF JULY 1, 1934, AND JULY 1, 1939.

17 SOUTHERN STATES

State	1934	1939	Per Cent Increase
Alabama	8	101	1162.5
Arkansas	3	85	2733.3
District of Columbia	8	18	125.0
Florida	3	56	1766.7
Georgia	17	89	423.6
Kentucky	75	91	21.3
Louisiana	7	45	542.9
Maryland	39	83	112.8
Mississippi	2	88	4300.0
Missouri	14	57	307.1
North Carolina	34	221	550.0
Oklahoma	3	46	1433.3
South Carolina	....	81	.....
Tennessee	43	95	120.9
Texas	3	45	1400.0
Virginia	12	102	750.0
West Virginia	14	48	242.8
Total	285	1351	374.0

Table 4

STATE HEALTH DEPARTMENTS ENGAGED IN THE FREE DISTRIBUTION OF DRUGS FOR THE TREATMENT OF SYPHILIS TO INDIGENT OR ALL CASES AS OF JUNE 30, 1935, and JUNE 30, 1939.

17 SOUTHERN STATES

State	Indigent Cases Only		All Cases	
	1935	1939	1935	1939
Alabama	yes	yes	no	yes
Arkansas	no	yes	no	no
District of Columbia	yes	yes	no	no
Florida	yes	yes	no	no
Georgia	yes	yes	no	yes
Kentucky	yes	yes	no	no
Louisiana	no	yes	no	no
Maryland	yes	yes	yes	yes
Mississippi	no	yes	no	no
Missouri	no	yes	no	no
North Carolina	no	yes	no	no
Oklahoma	yes	yes	no	no
South Carolina	no	yes	no	no
Tennessee	yes	yes	no	no
Texas	no	yes	no	no
Virginia	no	yes	no	yes
West Virginia	yes	yes	no	no
Total departments with free distribution	9	17	1	4
Per cent increase	88.8		300.0	

Southern states and in several instances presented to the law-making bodies to test the reaction to the proposed legislation. Detailed analysis of this material is presented in *Table 5*.

Progress has been made in the training of personnel in venereal disease control. In the Southern states there are four institutions offering postgraduate courses in this field. These are: Johns Hopkins Medical School, Baltimore, Maryland; Howard University Medical School (negro), Washington, D. C.; Vanderbilt University Medical School, Nashville, Tennessee; Louisiana State University Medical Center, New Orleans, Louisiana. In addition, instruction in the clinical management of syphilis and gonorrhea can be obtained at the Hot Springs, Arkansas, Medical Center operated by the U. S. Public Health Service. The state venereal disease officers have all received special training for their duties and many clinicians and nurses have taken advantage of this opportunity to perfect themselves in modern venereal disease control methods. There are still too few physicians and nurses, however, with reasonably adequate training in the field of venereal disease control.

All states offer free laboratory service for the diagnosis of syphilis. The serologic evaluation studies conducted by the U. S. Public Health Service and the American Society of Clinical Pathologists have been of value in improving the specificity and sensitivity of the serodiagnostic tests for syphilis and all of the Southern states have participated in these studies. In turn, many are planning to standardize performance of these tests in branch or other laboratories, with a view toward certification by the central laboratory. The plan of delayed darkfield examination has not been received too well, but when used properly is considered a worth-while service in the diagnosis of early syphilis. Direct darkfield examination service is available in varying degrees with many clinics equipped with darkfield apparatus. This important diagnostic procedure is being extended, both through laboratories and clinics. In some states private physicians can avail themselves quickly of this service, since the darkfield equipment is placed in accessible areas.

In every Southern state, either full-time or part-time workers are engaged in case finding and case holding, that is: (1) locating sources of infections and contacts of patients and persuading them to come in for treatment, and (2) returning the patients who have lapsed in their treatment to clinic or physician. Some clinics have developed excellent contact tracing methods, and report successful investigations of numerous epidemics of early syphilis. Not yet, however, have all venereal disease control programs taken advantage of this important case finding procedure. Clinics exist where epidemiologic investigation is not engaged in at all. Integration of intelligent case holding and case finding procedures in syphilis control with generalized public health nursing programs has been accomplished in several of the states and is rapidly becoming the policy in a few of the state health departments.

Data are not available to compare 1935 and 1939 state and local financial support for syphilis control programs. All states in the area have either appropriated or allotted funds for venereal disease control. These, together with local funds, are used to match, on a cooperative basis, the Federal venereal disease allotment. In a few instances, notably in North Carolina and Mississippi, specific ear-marked appropriations have been made by legislatures for venereal dis-

Table 5

STATES WITH LAWS FOR COMPULSORY PREMARITAL AND PRENATAL EXAMINATIONS FOR SYPHILIS AS OF JUNE 30, 1935, AND JUNE 30, 1939.

17 SOUTHERN STATES

State	Premarital Laws		Prenatal Laws	
	1935	1939	1935	1939
Alabama	no	no	no	no
Arkansas	no	no	no	no
District of Columbia	no	no	no	no
Florida	no	no	no	no
Georgia	no	no	no	no
Kentucky	no	yes[1]	no	no
Louisiana	no	no	no	no
Maryland	no	no	no	no
Mississippi	no	no	no	no
Missouri	no	no	no	no
North Carolina	no	yes	no	yes
Oklahoma	no	no	no	yes[3]
South Carolina	no	no	no	no
Tennessee	no	yes[2]	no	no
Texas	no	no	no	no
Virginia	no	no	no	no
West Virginia	no	yes	no	no
Total states with laws	....	4	....	2
Per cent increase		....		....

1 Effective March 1, 1940.
2 Effective July 1, 1941.
3 Only with consent of woman or at her request.

ease control. Ear-marked local appropriations have been made also by counties, communities and cities. This indicates a sound public reaction to the problem.

Active educational programs have been engaged in by all of the states. Free pamphlets and brochures, radio talks, press articles, motion pictures, popular talks and lectures and other educational approaches have been utilized to acquaint the public with the venereal disease problem and methods of control. Increased financial support is one evidence of a more favorable public sentiment influenced by educational activities. An enlightened public should be kept informed of advances and trends in syphilis and gonorrhea control and the present keen interest maintained. Skilful direction of educational activities should be an important element of the syphilis control program.

SUMMARY

Advances in syphilis control have been made during the period 1935-1939 in the Southern states where the problem admittedly is the greatest. Funds derived from the provisions of Title VI of the Social Security Act and the La-Follette-Bulwinkle Bill have enabled marked expansion to take place in venereal disease control programs throughout the area. A good start has been made and there is every reason to believe that control of syphilis will continue to go forward. A few of the outstanding accomplishments are listed:

(1) All of the Southern states have either a separate division or a subdivision of venereal disease control in the state health department. In June, 1935, only four of the seventeen had such administrative organization.

(2) Twelve of the seventeen states in June, 1939, had one or more full-time venereal disease control officers in comparison with two in June, 1935.

(3) All Southern states engage in the free distribution of drugs for the treatment of syphilis to indigent venereally infected individuals. Four states distribute drugs for the treatment of all. In 1935 only nine states distributed drugs for indigents and only one, Maryland, for all.

(4) Serodiagnostic tests for syphilis are free in all of the Southern states and have been improved as a result of the serologic evaluation studies. Equipment for the darkfield diagnosis of early syphilis is more freely available than formerly, but is not yet utilized satisfactorily.

(5) There has been an increase in the number of syphilis cases reported to state health departments by 162.3 per cent during the past four years.

(6) There has been an increase in the number of clinics for the treatment of venereal diseases from 285 in 1934 to 1,351 in 1939.

(7) Epidemiologic investigation of early and some other cases of syphilis is performed to some extent in all states. The efficiency and value of these investigative procedures have been well demonstrated by a number of health departments during the last four years. Clinics generally, however, do not take advantage of this practice of case finding to the greatest extent.

(8) All Southern states have either allotted or appropriated directly state funds for the control of venereal diseases. Most states and local governments have not yet appropriated enough funds to operate properly an adequate control program.

(9) Educational programs have been projected in every state. A favorable public sentiment toward the problem of venereal disease is believed to exist, though this should be cautiously sustained by skilful methods of approach to the public consciousness.

(10) Four universities in the Southern states offer special training courses in venereal disease control. In addition clinical training can be obtained at the Hot Springs, Arkansas, Medical Center. Physicians, nurses and social workers have received training at these centers, but many more are needed.

(11) Four states now have compulsory premarital and two compulsory prenatal examinations for syphilis.

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DISCUSSION (*Abstract*)

Dr. A. L. Gray, Jackson, Miss.—This discussion of the comprehensive paper by Dr. Heller is to take the form primarily of an outline of the venereal disease control program in Mississippi and the progress made in recent years in its development. A tremendous job has been undertaken in seriously combating syphilis and gonorrhea. Fortunately, public sentiment has been molded strongly behind the program.

In Mississippi, local financial participation is deemed essential to permanency of the program, and on this

principle the control program is being developed. It is expected to expand the program only to the extent that state and U. S. Public Health Service funds are augmented by county, city, and individual contributions. During the present budget year, there has been provided approximately $54,000 by county and city governmental agencies, and $50,000 by the State Legislature, in addition to the allotment under Title VI. During the fiscal year 1939-1940, a total of $250,000 is available from state, U. S. Public Health Service and local agencies for venereal disease control.

The program in Mississippi is directed at education, case finding, treatment of indigent and low income groups and case holding. It is being integrated as a part of the regular county health department program, and intensive work is not anticipated except in counties having full-time health service. In fact, venereal disease control is influencing many counties to establish full-time health service.

Direction of the control program is a part of the function of the Division of Preventable Disease Control and is in charge of a full-time supervisor in that Division assisted by a surgeon of the U. S. Public Health Service. Program planning, budgetary, and personnel matters are worked out through close cooperation between the Divisions of County Health Work and Preventable Disease Control.

Counties in which the work is being carried on are required to provide funds for the specific purpose of venereal disease control, in addition to the local funds provided for general health service. In this regard, there are approximately thirty-three counties at present in which intensive programs are being conducted. These counties have provided from $100 to $4,500 per county for this purpose, depending upon the need and the ability of the county to provide funds. Such funds, in addition to State and U. S. Public Health Service funds, are used to set up clinic, case finding, and follow-up services through the addition of public health nurses, clerical workers, and local physicians for part-time clinic service.

Most of the medical service rendered in clinics is by local physicians who are paid at the rate of $3.00 per clinic hour for their services in administering treatment. Local health officers do most of the physical examinations and classification of cases. The health department personnel interviews the clinic patients, makes clinic set-up, prepares records, and attends to case holding and case finding duties.

Progress in the Mississippi program, especially during the past eighteen months, is shown by the following facts: in 1934 there were two venereal disease treatment clinics in operation, and at present there are approximately one hundred and thirty such clinics. The present clinic load is approximately 10,000 cases. In 1934, no funds were provided from any source and specifically ear-marked for venereal disease control in the State, but in the present fiscal year there is available approximately $250,000 from U. S. Public Health Service, State and local sources, provided specifically for this purpose. A tremendous increase in case finding is shown by the fact that in the fiscal year 1934-1935, 46,468 specimens were examined, while in the fiscal year 1938-1939, 139,364 were done by the State Hygienic Laboratory.

Early in the fiscal year 1938-1939, the State Board of Health began distribution of drugs to private physicians for indigent cases, and early in the present fiscal year, free drugs were made available to physicians for their cases without regard to the financial status of patients. In the first quarter of the present fiscal year, this resulted in the distribution of approximately 18,300 doses of arsenicals, 18,000 doses of bismuth, and 17,000 ampules of distilled water to private physicians, at a cost of about $4,000. This drug distribution is through local health departments in counties having full-time health service, and directly from the State Board of Health in part-time counties.

Personnel training in venereal disease control is a feature of the program in Mississippi. Eight full-time health officers, eighteen private physicians, and six public health nurses are receiving special training in venereal disease control in this fiscal year. Serologists and technicians are receiving training from time to time in serologic work and darkfield technic.

Because of the large negro population in Mississippi, the problem of venereal disease control is a tremendous one which will require an annual expenditure of between $500,000 and $750,000 over a fifteen-year period to reduce the incidence of the venereal diseases to a respectable level, if there is such a level above zero. Mississippi has approximately 300,000 cases of syphilis alone.

Our program is well under way in Mississippi as in other Southern states, but only a beginning has been made. Attention in the future will be shifted toward infectious syphilis and away from latent cases which are not likely to become infectious. Professional and lay education must have an increasing place in the program if efforts are to result in ultimate control.

Dr. Frank Roberts, Memphis, Tenn.—The training of personnel for this work should be stressed. Demand on the part of the public and on the part of health departments for this work is heavy, and every effort is being made to secure competent persons to take these programs in hand. As every one knows, there is an acute shortage of trained people in this field. Such a combination of circumstances, great demand and shortage of supply is not without danger. There is constant temptation to employ mediocre talent when good talent is not immediately available. In the long run such a course will prove disastrous.

The problem of syphilis is present, but we must remember that it has been present for quite a few years, and if there are not enough well trained persons to attack the problem, then we should train them. As Dr. Heller pointed out, training centers have been set up and the training of personnel is a very vital part of the program. If the efforts now being expended are not sufficient to secure the personnel, then these efforts should be increased. Syphilis control funds cannot be spent better at this time than in the training of workers, even should it require the postponement of the actual operation of clinics and diagnostic centers.

Those in charge of the programs of syphilis control should be trained and experienced in general public health work. The syphilis problem is not just the problem of getting antisyphilitic drugs into the diagnosed cases. Epidemiologists are required and the nurses who follow up the clinic cases should not be "syphilis nurses," but general public health nurses. Those who carry on the educational campaigns must master the technic of public health education.

I believe most firmly that the syphilis problem cannot be separated from the other public health problems, but it presents many features that require expert and

special knowledge. This expert service should be made available before attempting to attack.

Dr. W. H. Y. Smith, Montgomery, Ala.—In Alabama our weakest link today is case holding and case finding. With the money that we have received from the United States Public Health Service, there is not sufficient money to employ an additional nurse in each county to take care of case holding and case finding activities. So the progress we have developed consists of four nurses who are loaned out to the individual counties to demonstrate to the nurses in these counties case holding and case finding activities and how to include these activities in the general nursing program.

Dr. Heller (closing).—It must be remembered that my data referred to June 30, 1939, and the venereal disease program are moving so fast and going so well that by the time this talk is presented we are about five miles ahead of things.

PUBLIC HEALTH ASPECTS OF THE TREATMENT OF CONGENITAL SYPHILIS IN A SOUTHERN CITY*

PRELIMINARY REPORT BASED ON THE TREATMENT OF 121 INFANTS WITH CONGENITAL SYPHILIS USING STOVARSOL BY MOUTH AND A FOLLOW-UP OF 832 INFANTS AT SIX MONTHS OF AGE BORN OF SYPHILITIC MOTHERS

By DAVID W. GOLTMAN, M.D.
Memphis, Tennessee

The City of Memphis had the highest infant mortality rate during the years 1933-34 of any city in the United States in its population class. Because of this fact an investigation was made by Dr. Ella Oppenheimer,[1] of the United States Children's Bureau, at the request of all parties in the community interested in child welfare. From this study has evolved a department of maternal and infant hygiene in the city health department which is attempting to carry on preventive pediatrics among the indigent in the community in as systematic a manner as possible. Syphilis is a well-known cause of stillbirths and premature births, and even though deaths attributed to it on death certificates are relatively few, in many instances congenital syphilis is unrecognized and is the debilitating and predisposing cause of death where another illness supervenes. Therefore, it was natural that Dr. Oppenheimer should include in her recommendations the development of increased facilities for the treatment of syphilis, particularly among pregnant women and among children.

A study made by Reinberger and Toombs,[2] of the Obstetrical Department of the University of Tennessee, covering a period of ten years from 1922-1932, showed that 94 per cent of 1,000 syphilitic prenatals studied, received treatment during the course of their pregnancies, and that 50 per cent of them began treatment during the first trimester and 27 per cent began treatment during the second trimester. This survey attested to the apparent adequacy of our antepartum treatment of syphilis, but we felt that a special clinic was needed in the city for the study and treatment of early congenital syphilis in order to take some of the load off the general adult syphilis clinic of the outpatient department, where it was formerly treated. Such a special clinic was started by Dr. Beulah Kittrell† and myself in June, 1936. It was established independently of our outpatient department. In a few months it was well enough known to receive all referrals of early congenital syphilis from the newborn service, pediatric wards, and pediatric outpatient department of the John Gaston Hospital. It was automatically limited to babies under 2 years of age so that our problem could be confined to the handling of the disease during infancy. We proceeded with the thought in mind that effective treatment during the first two years of life would eliminate in large measure the necessity for treating older children. A long range program was necessary, since it was decided that we try to examine every baby born of a syphilitic mother clinically and serologically at six months of age and every six months thereafter until it attained the age of puberty. This tremendous task was begun with the disturbing thought of Stokes[3] in mind that our antepartum treatment methods might be simply converting early infantile into tardive heredosyphilis. To accomplish the job of getting babies back for serologic check-up whose mothers have had fairly adequate treatment during pregnancy requires continuous education of the public health nurses to its necessity. They in turn carry the message to the mothers in their districts.

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*From the Department of Pediatrics, University of Tennessee College of Medicine, and the Division of Maternal and Infant Hygiene, Memphis Health Department.

†Then Director of Maternal and Infant Hygiene.

"Six months of age not only means a diphtheria shot at the well baby clinic, but if the mother took shots while she was carrying the baby it means a trip to the special clinic so the specialist can examine the baby and make sure it is all right."

The public health nurse is absolutely indispensable in a program of this type in any city regardless of size.

During the three-year period under consideration from June, 1936, to June, 1939, 1,878 syphilitic prenatals were admitted to the maternity clinic at John Gaston Hospital. Only 88, or 4.1 per cent, were white. In the same length of time we have begun treatment on 121 infants for congenital syphilis. These 121 infants were born of 117 mothers, 77 of whom received no treatment at all during the course of their pregnancies. However, 40 of these untreated patients were nonclinic cases. The 40 patients in the group of 117 who received some treatment were inadequately treated, with few exceptions, because of late or irregular clinic attendance. During the past three years serologic study has been done at six months of age on 832 infants born of the 1,878 syphilitic mothers who registered with the Obstetrical Department of the University of Tennessee. Roughly about 50 per cent of the babies born of syphilitic prenatals who have delivered in the three-year period under consideration have been brought back for serologic check-up. Some have been rechecked three or four times. The treatment that the mothers of these babies received was deemed fairly adequate. The gratifying part of this follow-up is that only 3 babies in this group of 832 had positive serology at six months of age. No baby with negative serum at six months has become positive when checked subsequently. This coincides with the observation of Roberts[4] that if a baby has not definite evidence of syphilis by the age of four months, in practically all instances it is not syphilitic. The course of antepartum syphilis treatment prescribed in Memphis at the beginning of this study was 8 injections of neo and 20 of bismuth. It was rare, indeed, to find a colored mother who had taken the total number of injections prescribed. Fortunately we found that about 8 injections of neo and 5 of bismuth was sufficient treatment in most cases to assure the birth of a viable nonsyphilitic infant if begun by the fifth month. All mothers who have had treatment for syphilis at any time are treated with each pregnancy regardless of the status of their serologic test. Pointing out that this is necessary, Cole[5] states that during pregnancy showers of spirochetes may be thrown into the blood stream even though the maternal syphilis may have been acquired years before.

Another thought in starting a program to handle the problem of early congenital syphilis was to make it as all-inclusive as possible and to correlate it with the general infant hygiene program prevalent in the city. In order to do this, discharge slips on all babies delivered of syphilitic mothers at the John Gaston Hospital are collected each day by the nursing supervisor of infant hygiene. The amount of treatment which the mother received during her pregnancy is supposed to be written on them. They are gone over each morning by the director of infant hygiene at the Health Department. If it is thought that the mother has been treated inadequately she is instructed to bring her baby to the special clinic at four weeks of age by the nurse in her district who gives postpartum care. They are then followed until the diagnosis of syphilis is established or ruled out. Problem babies who fail to thrive are sent to the clinic because syphilis in many instances is the cause of their failure to do well. Public health nurses have been taught that every baby with a rash is a suspect and consequently one may see everything from scabies to ammoniacal ulcerations on a clinic day, but some of them turn out to be syphilitic. Since practically all of our patients are colored, whose economic circumstance is poor at best, clinic visits had to be kept at a minimum. We hoped to accomplish this with the use of stovarsol by mouth in the treatment of the disease. It was felt that a higher return rate would be assured than if injections were used. Also, numerous favorable reports appearing in pediatric literature in preceding years influenced this decision.[6 7 8 9 10]

PLAN OF TREATMENT WITH STOVARSOL

The drug is given in 9-week courses with a 4-week rest period between each course, during which time no other form of antisyphilitic treatment is given. The maximum daily dose of the drug used is 0.01 gram per pound of body weight. During the first week, one-fourth of this amount is given; in the second week one-half of this amount; in the third week three-fourths of this amount, and from the fourth through the ninth weeks the maximum daily dose is prescribed. The drug is dispensed suspended in distilled water. During the first three weeks of treatment, enough drug is given to last

for one week suspended in 60 c. c. of water, a teaspoonful being given twice a day. From the fourth through the ninth weeks a 2-weeks supply is given suspended in 120 c. c. of water so that only bimonthly visits are necessary during the last 6 weeks of each course. We feel that it is safer to give the drug in water with instructions to give a teaspoonful twice a day than to dispense it in tablet form with the attendant necessity of breaking the tablets to administer the proper amount. No untoward effects have been noted during the past three years from the administration of the drug in this fashion, although the research department of Merck & Co., the manufacturers of the drug, advised against it because of possible variation in the amount of drug suspended in each teaspoon. This is the way the drug is given both on the children's ward and on the newborn service at John Gaston Hospital.

In order to warn mothers of possible untoward effects, they are given printed slips at each clinic visit which tell them to discontinue the drug if vomiting, diarrhea, skin rashes, red urine or illness supervene. Most observers point out the necessity for doing routine urinalyses where stovarsol is being used. Through a grant of money for clinical research from the University of Tennessee, we obtained a technician for a period of six months to do urinalyses on each baby every two weeks and blood counts at the beginning and end of each course of treatment. Evidence of kidney irritation appeared in only one instance. Hence we decided to dispense with this procedure as a routine because it was time-consuming to catheterize or tube babies at each clinic visit. The rest periods between courses probably preclude any serious kidney damage and allow for ample elimination of the arsenic. Now urinalyses are done only when indicated.

DIAGNOSIS

The diagnosis of congenital syphilis is often a difficult matter, and there is great variability of opinion in different sections of the country regarding the proper course to follow in handling a disease in which the diagnostic criteria are not definitely established. In many instances treatment is instituted on clinical evidence alone with negative serologic and roentgenologic findings. Sometimes treatment is begun because of prematurity, as in the case of Rambar,[11] who treats all premature babies born of syphilitic mothers from Sara Morris Infirmary of Michael Reese Hospital on the assumption that syphilis is the probable cause of the prematurity. In the beginning of our experience with the handling of the disease we were influenced by this report and adopted the same policy. After a few months a more middle-of-the-road course was followed. If the mother has had adequate treatment in our opinion the premature or full-term infant is followed closely and no treatment is given unless the diagnosis of syphilis is definitely established. This is in line with the opinion of Black,[12] who says:

> "It is certainly not malpractice to insist upon a positive diagnosis before undertaking the treatment of syphilis. Indeed, one of the important axioms of the proper management of this disease is that the diagnosis must be established before treatment is instituted. I have no argument with those who advocate treatment on strong or even on weak suspicion of the presence of the disease, but I do contend in the interests of science and the advancement of our knowledge of the nature of the infection that a sharp distinction should be drawn between a positive and a presumptive diagnosis of congenital syphilis."

During the past year, x-ray pictures have been taken of the long bones of babies born of syphilitic mothers on the newborn service at the John Gaston Hospital. A rather frequent finding has been a dense zone at the ends of the long bones previously described by Stafford McClean.[13] This finding is probably not of great significance and subsequent close follow-up of these infants is necessary in order to determine whether these bone changes clear up or persist with the development of other luetic bone finding. This type of investigation is being carried out here at the present time and will probably be reported on in the future. Since injections of bismuth have been given in the past after routine injections of neo, the question naturally comes up as to whether these dense zones represent fetal absorption of bismuth administered to the pregnant mother. A comparison with long bone x-rays taken on a series of babies born of nonsyphilitic mothers would help to clear this point.

GENERAL CONSIDERATIONS ABOUT STOVARSOL

As previously stated, stovarsol has been given to 121 infants in our clinic. In addition to this, it is used almost routinely at John Gaston Hospital both on the newborn nursery and on the children's ward. In many instances on the newborn service it has been started a few days after birth on syphilitic prematures. The drug is tolerated well by them. No severe toxic manifestations have been noted. Occasionally the drug has been discontinued temporarily because

of a febrile illness, questionable scarlatiniform or eczematous rashes, vomiting or diarrhea. However, these are such common findings in pediatric experience during infancy that the role of the drug in their production was ofttimes very questionable. In no instance has it been felt necessary to discontinue the drug permanently because of untoward effects from its use. Skin lesions usually disappeared within two to four weeks after the beginning of treatment and the healing of bone lesions has been most gratifying. In cases where the drug was given conscientiously, reversal of the serologic test normally occurred on the average at the end of the second course. Improvement in the general appearance and well being of the child and increase in weight were the general rule where treatment was given with regularity. Rises in the red count and hemoglobin values usually accompanied the general improvement. The eosinophilia frequently seen in congenital syphilis was a fairly constant finding in our cases. We have continued to give the drug until the child is two years old with a minimum of three negative serologic tests as the basis for its discontinuance. In a few instances treatment has been extended beyond the second year where the child did not come to the clinic sufficiently early to receive an adequate amount of treatment prior to this time. In several cases where reversal of the serologic test did not occur at the end of three courses, bismuth salicylate in oil was given between courses of stovarsol.

STATISTICAL DATA

Since the start of this clinic three years ago, stovarsol has been given to 121 babies. Of these, 105 were colored and 16 white. We have lost track of 35 because of change of address. Many of these patients came in from out of town, were delivered here and then moved away. Only 53, or 43.8 per cent, of the babies have attended the clinic regularly since its inception. In 24 instances clinic attendance has been very sporadic. This shows rather clearly that the high return rate that we hoped to get by the use of stovarsol has not been realized. Poor economic circumstances combined with the difficulty of getting someone to bring the baby where the mother is a wage earner are the major causes of this condition. In the group studied, 9 babies have died. In 3 instances death was caused by prematurity and malnutrition and 2 died of tuberculosis. Pertussis, bronchopneumonia and influenzal meningitis caused 3 of the deaths. A baby of 7 weeks died suddenly at home, and whether stovarsol played any causative role is very questionable.

When treatment was instituted, 97 of the 121 babies had positive serologic tests and 24 had negative tests. The reason treatment was started in those with negative sera was prematurity (8 cases), bone evidence (5 cases), very inadequate or no treatment of mother (5 cases), clinical evidence (3 cases), twins (3 cases). It is interesting to note that in 3 sets of twins one of each set had a positive serum and the other a negative. This possibility has previously been described in multiovular twins by Jeans and Cooke[14] with the breaking down of only one of the two placental barriers by spirochetes. In 27 instances out of 117, the mother's antepartum blood test was negative so that in 23 per cent of our cases the maternal syphilis was apparently contracted after the original maternity clinic visit. Because of this fact, routine checks are being done now on all mothers delivered at John Gaston Hospital, and this will probably be extended to home deliveries as well.

Because of the relatively short period of time (three years) that the clinic has been in operation, only 12 children have received stovarsol for a sufficient period of time to be discharged from the clinic, and 11 of the 12 have negative sera. Reversal of the serum test occurred on the average at the end of two courses and the group received an average of 5.7 courses of stovarsol. One is Wassermann-fast even after intensive bismuth therapy in addition to the stovarsol. All are clinically well and are being checked at regular intervals. There are 45 babies under treatment at the present time.

DISCUSSION

Since February, 1939, a comprehensive syphilis program has been in progress in Memphis under the direction of Dr. G. F. McGinnes. Our clinic has been incorporated into this new setup in its original form. The effort to follow by serologic examination at six months of age all babies born of syphilitic mothers will be continued. Subsequent follow-up after six months of age will also be continued, but less frequently than the originally planned six-month intervals. The fear of the development of tardive heredosyphilis is probably a hang-over from pre-Wassermann days when the early infantile syphilis that probably preceded it was unrecognized and hence untreated. The poor return rate that has been secured with a single clinic limited to babies under 2 years makes it apparent that greater

availability of clinic to patient is necessary in the handling of congenital as well as adult syphilis. Poverty outweighs the advantage of any single simple method of treatment, such as the use of stovarsol by mouth. The drug, however, has proven itself in our limited experience to be very effective when given regularly.

SUMMARY

(1) Stovarsol by mouth has proven effective in the treatment of congenital syphilis in a clinic limited to babies under 2 years of age.

(2) The use of the drug has not produced the high return rate anticipated.

(3) Some of the public health aspects of this difficulty have been discussed.

(4) The results of a follow-up at six months of age of 832 infants born of syphilitic mothers are recorded.

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THE TREATMENT OF CONGENITAL SYPHILIS*

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Since 60,000 infants[1] each year are born in this country with congenital syphilis, the need for an adequate and completely effective plan of treatment becomes an issue of major importance, meriting the attention of the obstetrician in the prevention of this high incidence, and of the pediatrician and general practitioner in its recognition and treatment. Whipple and Dunham,[2] in an analysis of reports on "over 2,000 children diagnosed as syphilitic and treated by well-known methods before the age of 2 years," found that "only one-fourth of the children were adequately treated and followed long enough to determine the results." However, the modern technic of treatment has been found sufficiently effective by Schamberg and Wright[3] that with early recognition and complete treatment of the condition, it would not require many years to eradicate the disease from the face of the earth. Since the introduction of the more intensive combined and continuous methods of treatment, the incidence of syphilis is appreciably declining, particularly in the Scandinavian countries.

Clinical signs and symptoms of syphilitic infection being absent in upwards of 50 per cent of cases of maternal lues, the separate histories taken from the mother and father are valuable, but the routine Wassermann testing of every pregnant woman immediately upon the diagnosis of pregnancy is indispensable, regardless of clinical indications and the social or financial status of the individual. The incidence of syphilis was 5 per cent in 25 prenatal clinics in Philadelphia making routine serologic tests, but only 1 per cent in eleven prenatal clinics employing the test merely as indicated.[4] Pregnancy as a frequent cause of false positive Wassermann reactions has been discredited, and when a rare nonspecific reaction appears, it is always in the last weeks of pregnancy.

Transmission of syphilis to the fetus depends on the stage of the disease in the parents at the time of conception. If either parent is suffering from secondary symptoms at the time of conception, infection of the offspring is almost certain.[5] If treatment has been instituted prior to conception, or if the disease is in the more latent tertiary stage, the fetus may escape infection. As a general rule, the more recent the infection in the parent, the greater the hazard of transmission and the more severe form the transmitted disease will assume in the fetus. The fact of transmission of syphilis via the mother is now universally accepted and Colles' law[6] that the mother of a syphilitic infant will not become infected by contact with it merely proves a relative immunity in the mother because of latency of the disease through previous infection. Third generation syphilis, heretofore generally discredited, has been conclusively proven in the offspring of two families by Rosenbaum and Faulkner.[26]

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Pathologic studies have failed to disclose histologic changes in the assumably infected fetus before the fifth month of pregnancy, so that prompt full treatment of the infected mother beginning between the first and fifth months of pregnancy will insure a viable seronegative fetus with none of the luetic stigmata. Treatment of the mother begun even late in pregnancy materially reduces the incidence of infection in the offspring.[7] If the offspring of untreated syphilitic women are permitted to go without specific treatment until they are clinically syphilitic, 56 per cent will die in the first three months of life, whereas if all are treated immediately after birth, the mortality rate will be only 16 per cent.[8] Comparing 100 treated with 100 untreated women, it was found[9] that in the untreated group premature births were two times, stillbirths three times, abortions seven times, and infant deaths in the first ten days of life nine times more frequent than in the treated cases.

The question of treatment of the syphilitic mother during subsequent pregnancies is of vital importance in the prophylaxis of congenital syphilis. Ingraham and Kahler[4] contend that our present knowledge of the curability of syphilis does not warrant permitting such women to omit treatment in any pregnancy following infection. In 1938, the Cooperative Clinical Group recommended that every syphilitic mother be given "early and adequate treatment throughout every pregnancy."

Recognition of congenital syphilis in the newborn is often a difficult problem, especially since positive clinical signs are frequently absent during the newborn period in the offspring of a syphilitic mother. In a series of 56 infants born of syphilitic mothers, Davies[10] was able to detect congenital syphilis clinically in only one infant during the newborn period. The dark-field examination of scrapings made from the inner vessel wall of the umbilical vein may reveal the presence of spirochetes with negative placental findings and a negative Wassermann on blood from the umbilical vein.[12 28]

A positive Wassermann test in the newborn is not of itself positive proof of syphilitic infection of the infant, and it may merely indicate the continued presence of a positive serologic reaction in the mother. However, seropositive newborn infants present a higher incidence of congenital syphilis than seronegative newborns, so that serologic tests should be repeated in all offspring of syphilitic mothers at regular intervals until the infant is between 5 and 6 months of age. A pertinent observation by Davies[10] is that the development of two or more strongly positive blood tests after a negative test points strongly to actual infection.

The diagnosis of congenital syphilis should not be dismissed in the case of an infant born of a syphilitic mother for at least six months of negative Wassermanns. Even the remotest clinical suspicion of congenital syphilis detected in the newborn is ample justification for continued intensive treatment of that infant regardless of the serologic reaction. X-ray films of the long bones, while frequently disclosing the typical picture of luetic bone changes in the newborn, do not exclude syphilis through absence of the characteristic changes.

Drugs used in the treatment of congenital syphilis include the arsenicals and the heavy metals. Since 1910, the trivalent arsenicals have been predominantly the drugs of choice in the treatment of syphilis. Of the trivalent arsenicals, arsphenamine, neoarsphenamine and sulfarsphenamine have been most generally and effectively used in the order named, while recently "mapharsen" is claiming the interest of many clinicians. Arsphenamine is administered intravenously, neoarsphenamine usually intravenously and occasionally intramuscularly, while the intraperitoneal route is now entirely abandoned. Sulfarsphenamine is administered intramuscularly and "mapharsen" intravenously. The pentavalent arsenicals used are acetarsone administered orally and tryparsamid, given preferably intravenously, though also used intramuscularly.

The action of the arsphenamines is not directly upon the spirochetes, the specific spirocheticidal action being effected by oxidation of the arsphenamine.[11] This effect begins within 5 to 8 hours after administration and disappearance of the organisms occurs within the next twelve to twenty-four hours.[12]

Because of the difficulty of intravenous administration of arsphenamine in infancy and early childhood, and the danger of sloughing through leakage into the surrounding tissues, it is rarely used in childhood today, and sulfarsphenamine, as contributed by Voegtlin and co-workers[13] in 1922, has almost completely supplanted it. Factors other than ease of administration that make sulfarsphenamine especially adaptable are lack of tissue irritation when it is

given intramuscularly or subcutaneously, thereby minimizing pain, and its stable solution with low toxicity. Results obtained from its use in the treatment of syphilitic infants are increasingly favorable[13 14 15 16] both from the standpoint of clinical cure and reversal of the serum reaction. Jeans and Cooke,[15] after an exhaustive clinical study of the effects of the drug, could find no clinical evidence which proved it inferior to the original arsphenamine in producing serologic cure. Stokes and Behn[17] express the opinion that intramuscular injections of sulfarsphenamine produce as good results as intravenous doses of "606."

For routine use in congenital syphilis, sulfarsphenamine is given preferably intramuscularly in a dosage of 0.02 gram per kilogram of body weight. The favored plan of treatment involves the continuous use of six or eight weekly doses of sulfarsphenamine, alternating with six or eight weekly doses of the heavy metals, with no interruption by rest intervals.

Reactions following arsphenamine administration include the more frequent, immediate and fleeting nitritoid reaction, so called because of its resemblance to the effects of amyl nitrite; and the less frequent, more prolonged constitutional Herxheimer reaction, which develops within 8 to 12 hours after intravenous injection, and is usually accompanied by fever and intensification of symptoms referable to organs or tissues involved in the luetic process. The latter reaction usually appears after the first injection. It is not absolutely specific for syphilis, since it has been observed following intravenous arsenical administration in tuberculous subjects, in the other spirochetoses, notably rat-bite fever, and rarely after bismuth administration. Jeans and Cooke[15] have never observed a typical Herxheimer reaction in children.

A rarer complication and a chief cause of death from arsphenamine administration is hemorrhagic encephalitis. It usually occurs following the early doses of the arsenical employed, and appears 48 to 72 hours after the dose is administered. Generalized clonic convulsions with rising temperature usher in the syndrome, with hyperactive reflexes, early appearance of coma, and death within 24 to 48 hours from onset of symptoms. Stokes[12] reports one case following neoarsphenamine which terminated fatally; Lees had three recoveries in seven cases; while Jeans and Cooke[15] observed five cases of postarsphenamine encephalitis, two of which terminated fatally following administration of neoarsphenamine. Of the three recoveries, one had received arsphenamine and two had received sulfarsphenamine.

The most serious cutaneous reaction following arsphenamine administration is exfoliative dermatitis, this condition ranking next to hemorrhagic encephalitis in the fatalities due to the arsenicals. It is seen more often after sulfarsphenamine.

The hematopoietic system is involved in postarsenical reactions, and aplastic anemia, purpura and agranulocytosis may occur, aplastic anemia causing 5 per cent of postarsenical deaths.[12]

"Mapharsen," or arsenoxide, was synthesized by Ehrlich and Hata in 1910. Ehrlich assumed that the active principle of salvarsan was a product of the breaking down of salvarsan in the body, i. e., the "arsenoxide," which is actively spirocheticidal. Voegtlin and Smith[11] conclusively proved this action of the trivalent arsphenamines, though Voegtlin feared, as Ehrlich had originally, that arsenoxide might be highly toxic. Tatum and Cooper,[18] in 1934, reported the results of their investigation of the drug in the treatment of syphilis in experimental animals and their findings provided the basis for a clinical study by Foerster[19] and co-workers in 1935.

The results of Foerster's and subsequent clinical investigations indicate that "mapharsen" possesses high spirocheticidal power even in a dosage smaller than is required with the other arsenicals; that in early syphilis its effects are especially valuable; that healing of visible lesions was as rapid as in treatment with arsphenamine; reversal of serologic reactions is prompt and usually permanent. No nitritoid reactions occur. Howles[20] reported in 1938 his favorable impression of the intravenous use of "mapharsen" in prenatal and congenital syphilis, though the best results obtained in his comparative series were with combined alternating courses of "mapharsen" and bismuth subsalicylate.

Evidence is lacking to prove the value of "mapharsen" in cerebrospinal, cardiovascular and other late forms of syphilis, and reports of its use in congenital syphilis are too limited to permit of final judgment on this drug at the present time. The favorable results reported by all investigators[20 21] to date justify further use and careful observation of patients for an eval-

uation of the drug in its later and more prolonged effects.

Acetarsone is a pentavalent arsenical first prepared by Ehrlich and Hata in 1908, but not popularized for clinical use until 1921. Its chief value lies in its effectiveness by oral administration, thereby eliminating the pain and attendant difficulties of administration by needle. It is a white crystalline powder, odorless, with a slightly acid taste and is dispensed in 0.1 and 0.25 gram tablets.

Several plans of treatment by oral administration of acetarsone have been recommended, though the conservative plan of gradually increasing dosage recommended by Bratusch-Marrain[22] is most frequently used. This dosage is based on the weight of the child as follows:

First week, 5 mg. per kilogram body weight daily.
Second week, 10 mg. per kilogram body weight daily.
Third week, 15 mg. per kilogram body weight daily.
Next 6 weeks, 20 mg. per kilogram body weight daily.

Rest periods of 4 to 6 weeks alternate with the drug periods, a Wassermann reaction being

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	Age on Admission	Color	Sex	Blood Wassermann	Spinal Fluid Wassermann	Symptoms and Signs
L.A.V.	2 yrs.	White	F	2/22/39 Wass. Pos. Precip.—Pos. 10/12/39 Wass. Wk. Pos. Precip.—Mod. Pos.	Neg.	None pathognomonic of lues
M.L.V.	6 yrs.	White	F	2/22/39 Wass.—St. Pos. Precip.—St. Pos. 8/25/39 Wass.—St. Pos. Precip.—St. Pos.	Neg.	Interstitial keratitis left eye
M.D.	2 mos.	Negro	F	2/22/39 Wass.—St. Pos. Precip.—St. Pos. 7/21/39 Wass.—Neg. Precip.—Neg.	10/26/39 Neg.	Prematurity, snuffles, malnutrition, persistent crying, tenderness+swelling knees and wrists. Dehydration
L.J.	3 mos.	Negro	M	4/27/39 Wass. Precip.—St. Pos. 9/22/39 Wass. Precip.—Neg.	10/21/39 Neg.	Snuffles, hoarseness, fluid skin lesions
J.W.	2 mos.	Negro	M	5/ 3/39 Wass. Precip.—Pos. 10/13/39 Wass. Precip.—Neg.	10/26/39 Neg.	Skin lesions over buttocks, back, + extremities. Diarrhea.
F.L.S.	2½ yrs.	Negro	F	1/12/39 Wass. Precip.—Pos. 5/19/39 Wass. Precip.—Wk. Pos. 10/12/39 Wass. Precip.—Neg.	10/21/39 Neg.	Common cold. No signs of syphilis
R.F.	19 mos.	White	M	4/ 6/39 Wass. Precip.—St. Pos. 7/ 2/39 Wass. Precip.—St. Pos.	10/18/39 Pressure 8 mm. Cells, 450 Wass., pos.	Flaccid paralysis right side of body. Vomiting
R.E.	7 mos.	White	M	11/ 2/38 Wass. Precip.—St. Pos. 5/11/39 Wass. Precip.—Neg.		Snuffles, hoarseness, cough, difficulty in nursing. Thrush
J.P.	4 mos.	Negro	F	1/ 6/39 Wass. Precip.—St. Pos. 5/11/39 Wass. Precip.—Neg.	10/23/39 Neg.	Chronic rhinitis, cough, fever, loss of weight
E.G.	6 yrs.	White	M	10/ 3/38 Wass. Precip.—St. Pos. 9/28/39 Wass. Precip.—Pos.		Chronic rhinitis, hepatomegaly, impetigo
S.B.	22 mos.	Negro	F	4/ 3/39 Wass. Precip.—Pos. 10/12/39 Wass. Precip.—Neg.	4/ 3/39 Neg.	Inability to stand alone or walk. Peeling of skin, snuffles at birth
M.C.	20 mos.	White	M	1/19/39 Wass. Precip.—Pos. 10/22/39 Wass. Precip.—Neg.	10/26/39 Neg.	In December, 1938, because of rash on hands, was given "shots"
A.M.J.	7 mos.	Negro	F	5/22/39 Wass. Precip.—Neg. 6/14/39 Wass. Precip.—Neg.	10/12/39 Neg.	Extreme malnutrition, persistent coryza. Marked restlessness at night
E.M.J.	7 mos.	Negro	F	5/22/39 Wass. Precip.—Neg. 6/14/39 Wass. Precip.—Neg.	10/15/39 Neg.	Extreme malnutrition. Persistent coryza since birth

taken after every drug course until three successive negative reactions are obtained. Six months later a safety course of 9 drug weeks is recommended even in the presence of repeatedly negative Wassermanns.

Many are enthusiastic about acetarsone when administered in combination with a heavy metal, Rambar[23] and Baumbach[24] having given mercury during the rest periods of the Bratusch-Marrain plan of treatment. Others[27 28] have insisted that bismuth intramuscularly be used in the rest periods between courses of acetarsone.

Bratusch-Marrain reported 14 cures in a two-year observation of 23 children treated with acetarsone by mouth. Smith, Fried and Everhart[25] used acetarsone in 33 cases of congenital syphilis, with negative serologic results in 24 patients. The younger the patient treated with acetarsone by mouth, the greater the incidence of serologic reversal.

Tryparsamid, another of the pentavalent arsenicals, does not possess the high spirocheticidal action of the arsphenamines, but has the valuable effect of more complete penetration of the central

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X-Ray Long Bones	Evidence of Syphilis in Parents	No. Injections Sulfarsphenamine	Total Amount Sulfarsphenamine	No. Injections Bismuth Subsal.	Total Amount Bismuth Subsal.	Reactions
Negative for bone disease	Father has taken antiluetic treatment	11	1.9 gm.	18	.468 gm.	None
Negative for bone disease	Mother's blood reaction not known	11	2.7 gm.	16	1.04 gm.	None
Marked periostitis. Irregularity of epiphyseal lines	None	16	1.3 gm.	12	.182 gm.	None
Periostitis, irregular punched-out absence of bone, int. sides, prox. ends tibiae	Mother taking antiluetic treatment	11	.66 gm.	8	.104 gm.	None
Negative for bone disese	Both parents taking antiluetic treatment	11	.95 gm.	10	.13 gm.	None
Slight lateral bowing, both tibiae	Father, mother + three siblings taking antiluetic treatment	26	6.25 gm.	16	.624 gm.	None
Negative for bone disease	Mother Wass.—Neg. Precip.—Pos. Father Wass.—Neg. Precip.—Pos.	24	5.45 gm.	24	.832 gm.	Nodulation at site of injection
Periostitis of long bones	Mother Wass.—Neg. Precip.—Pos.	18	2.2 gm.	16	.26 gm.	Exitus 9/26/39 Question of hemorrhagic encephalitis
Irregularity epiphyseal lines both tibiae. Periostitis of tibial shafts	Mother taking antiluetic treatment	23	3.1 gm.	19	.325 gm.	None
Negative for bone disease	Mother taking antiluetic treatment	16	6.2 gm.	22	1 gm.	None. Albuminuria not aggravated by treatment
Long bones show changes at joints with evidence of periostitis suggestive of lues	Mother, 18 years, taking antiluetic treatment	8	1.35 gm.	8	.312 gm.	None
Negative for bone disease	Mother, 37 years, is taking "shots" at present (8th preg.). Fifth pregnancy stillborn. Sixth pregnancy miscarried at 6 weeks	11	2.1 gm.	8	.26 gm.	None
Negative for bone disease	Mother taking antiluetic treatment	10	0.9 gm.	8	.143 gm.	None
Negative for bone disease	Twins. Four previous pregnancies miscarried	10	0.9 gm.	8	.143 gm.	None

nervous system, hence its special indication in neurosyphilis. Tryparsamid is dispensed as fine white crystals readily soluble in water. A recommended dosage of 0.05 gm. per kilogram of body weight injected intravenously is administered once weekly, the solution being prepared under all the precautions necessary to arsphenamine. From 70 to 100 doses are usually necessary in each case, and the alternating or overlapping use of bismuth is advocated. The imminent danger of damage to the optic nerve should be borne in mind whenever tryparsamid is considered as a therapeutic measure.[12]

Stokes claims a 33 per cent favorable action clinically and serologically in the use of tryparsamid. Jeans and Cooke recommend its use in congenital syphilis when the spinal fluid remains positive after one year's treatment.

Of the heavy metals—bismuth, iodides, and mercury—bismuth is predominantly the drug of choice.

Its favorable action in the treatment of syphilis was first reported by Muller in 1922. This action is ascribed to a stimulation of tissue resistance against the spirochete. Bismuth is more actively specific and less toxic in its action than mercury, and is well tolerated by children in proper dosage. The kidneys act as the eliminative organs for both bismuth and mercury, therefore they should never be given together.

There are both water-soluble and oil-soluble compounds of bismuth, the water-soluble being administered two or three times weekly and the oil-soluble once weekly. The insoluble bismuth compounds are dispensed in oily suspensions. The usual dosage of bismuth is 2 mg. per kilogram of body weight.

Bismuth should never be administered intravenously, the only effective route of administration being the intramuscular route. Because of the comparative safety of the bismuth compounds, the slower rate of absorption and the less intense Herxheimer reaction, it is recommended that bismuth be used in the initial course of treatment in all florid or fulminating cases, some following this plan routinely in all types of cases. It has been observed that infants show less shock reaction from the arsphenamines when given preliminary treatments with bismuth preparations.

SUMMARY

Fourteen infants and children, six white and eight colored, aged 2 months to 6 years, were treated for congenital syphilis by alternating injections of bismuth subsalicylate in oil and sulfarsphenamine. The period of individual treatment extended from 5 months to 1 year. Seven of the patients were under one year at beginning of treatment and seven were 1½ to 6 years.

Treatment consisted of intramuscular injections of bismuth subsalicylate into the gluteal muscles at weekly intervals for 8 doses, followed by 8 doses of sulfarsphenamine administered weekly. No oral medication was used other than administration of cod liver oil.

All patients presented positive blood Wassermanns at the time of first observation except two colored twins, who were included in the series because of extreme malnutrition, persistent coryza, and a positive blood Wassermann with postpartal antiluetic treatment in the mother.

Syphilis in the parents was proven by recent positive Wassermann reactions followed by treatment in eleven of the series, and a positive reaction following an earlier course of treatment in the father of two of the children. In this family the mother's Wassermann was negative, while syphilis was not proven in another mother of one child in the series.

Symptoms and signs of congenital syphilis included snuffles and chronic rhinitis in 8 cases, skin lesions in 4, malnutrition in 7, hepatomegaly in 1, inability to walk or stand alone in 1, flaccid paralysis of the entire right side of body in 1 and interstitial keratitis in 1. X-ray examination of long bones revealed characteristic luetic bone changes in five patients.

Two hundred six intramuscular injections of sulfarsphenamine and 193 intramuscular injections of bismuth subsalicylate in oil were given with no reactions other than persistent nodulation at the site of injection in one patient and an unproven hemorrhagic encephalitis in another patient.

The maximum number of doses of sulfarsphenamine given an individual patient was 26, representing a total dosage of 6.25 grams sulfarsphenamine. The maximum number of doses of bismuth subsalicylate administered an individual patient was 24, representing 0.83 gram bismuth subsalicylate.

Reversal of the blood Wassermann reaction was obtained in eight of the twelve patients with positive reactions, or in 66 per cent of the series. Reversal of the blood Wassermann developed

in from 4 to 9 months under the continuous alternating sulfarsphenamine and bismuth subsalicylate intramuscular injections.

Of the four in which reversal was not obtained, one showed a modified reaction, the Wassermann being weakly positive and the precipitin test moderately positive. Two of the completely unchanged reactions presented in one case a meningovascular syphilis and in the other patient an interstitial keratitis. The third completely unchanged serum reaction occurred in a patient who had previously received partial brief periods of treatment, interrupted by a persistent and severe acute hemorrhagic nephritis.

Twelve patients in this series showed negative spinal fluid Wassermann reactions. The patient with meningovascular syphilis, whose fluid presented evidence of continued meningeal involvement in its increased pressure and increased cell count, showed a persistently positive reaction, while spinal fluid was never obtained from the fourteenth because of continued indifference of the parents. In spite of the continuously unchanged serum reactions in the patient with meningovascular syphilis, marked clinical improvement was noted in the improved nutritional state, the diminution of paralysis, and the greatly improved disposition and general psychic reactions.

The one fatality in the series occurred in a white male of 17 months under observation from the age of 7 months. Diagnosis in this case was established by a strongly positive Wassermann reaction and typical luetic periostitis of the long bones. Reversal of the blood Wassermann reaction developed after six months of sulfarsphenamine and bismuth therapy. Treatment was continued after serum reversal in order to complete the original plan of at least one full year of continuous treatment. An intramuscular injection of sulfarsphenamine was made in the gluteal musculature on September 22, 1939, and early on the morning of September 26 the patient became cyanotic, respirations were slow and labored and generalized convulsive twitchings were noted, especially in the facial muscles. Admitted to Charity Hospital at 10:30 a. m. in convulsions with temperature 96°, the convulsions became rapidly more violent, temperature rose to 108° and the patient expired in rigid generalized tonic muscular spasm at 2:35 p. m. While a gross postmortem anatomical diagnosis of acute encephalitis was made on inspection of the brain, this diagnosis was not confirmed by histologic examination and the cause of death remained undetermined. No histologic evidence of lues could be ascertained postmortem.

CONCLUSIONS

The system of treatment of congenital syphilis by continuous alternating courses of sulfarsphenamine and bismuth is presented in this small series of cases to endorse a rational and effective plan of treatment adequately administered. A comparative study of various plans of treatment was not undertaken.

All offspring of mothers who present serologic or clinical evidence of syphilis should have a blood Wassermann every month for the first five months of life, at the termination of which time a spinal fluid Wassermann should be obtained before declaring the infant nonsyphilitic.

The development of any suspicious clinical manifestation of lues in the infant is sufficient justification for continuous antiluetic treatment, regardless of serologic reactions.

Treatment of congenital syphilis is entirely effective both serologically and clinically when instituted early and applied intensively in full dosage of sulfarsphenamine and bismuth subsalicylate for a minimal period of one year.

The older the patient at the time of discovery of the prenatal syphilitic infection, the greater the difficulty in obtaining a serologic response to treatment, though clinical improvement is anticipated at any age in childhood.

Absence of clinical signs or symptoms should never be accepted as sufficient grounds for deferring further investigation for presence or absence of syphilis in the newborn whenever a suspicion of parental infection arises.

After a comparison of results obtained recently by the use of other arsenicals with the results obtained in our more orthodox plan of treatment, the conclusion is inescapable that success in the treatment of congenital syphilis is dependent largely on the amount rather than the type of arsenical administered, provided treatment is continuous, and courses of bismuth are alternated with courses of the selected arsenical.

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DISCUSSION (*Abstract*)

Dr. Walker L. Rucks, Memphis, Tenn.—Dr. Naef has given us a rather complete review of the literature relative to the drugs used in the treatment of congenital syphilis. All of us who have gone through the periods of mercury inunctions, arsenical injections and later the use of bismuth wonder sometimes if we know when a case of congenital syphilis is cured. A great many cases of congenital syphilis are symptom-free, but blood-positive even under the best of treatment. Most of us are of the opinion that the earlier treatment is begun during pregnancy the better chance we have of bringing into this world a syphilis-free child.

I wonder sometimes, in watching the negro, if there is not a certain amount of immunity acquired through syphilitic infection. We all feel that there are certain strains of spirochetes which have a predilection for attacking certain parts of the body. I have never seen a case of syphilis transmitted from the kitchen.

The study of congenital syphilis is an outpatient problem. In private practice we see one occasionally and these are not financially able to carry on the treatment.

Dr. Naef (closing).—The question of natural and inherited immunity to syphilis constantly engages the attention. Natural immunity to syphilis exists only in the lower animals except certain types of monkey, the rabbit and mouse. Non-syphilitic offspring are sometimes born of syphilitic mothers because of failure of the mother's lesions to discharge a sufficient number of spirochetes to infect the fetus. Such a fetus possesses no inherited immunity and remains as susceptible to infection as the offspring of a normal mother. No vaccine or serum has been obtained to date which has the slightest effect in conferring any degree of immunity.

Syphilis is a social problem in more ways than one. As it affects the child it is largely the problem of the underprivileged, included in which class are the underprivileged white children and a still larger percentage of the negro child population, who constitute the great majority of our cases. Our purpose in approaching the study was to be equipped with a more complete knowledge of the technic of treatment and its effects, since today the treatment has been rationalized and simplified. During the past summer a case was referred to me by a physician some 150 miles out of town. When the child presented, I was confronted with what at first glance appeared to be a typical syphilitic pemphigus as distinguished from the usual infectious pemphigus neonatorum. My impression as I reviewed the case was that the child was not syphilitic. It was up to me to prove the presence or absence of syphilis. The physician had already started mercurial inunctions, which had been used for about a week before I saw the child. The child was two weeks of age. There had been a previous birth of a child with exactly similar findings two years before, with death on the twenty-fifth day and an unproven diagnosis of syphilis. The obstetrician felt that the mother was syphilitic, though this was not proven in blood taken during the time of each pregnancy. The father's blood Wassermanns were repeatedly negative. My impressions in this case were further confirmed by a negative blood Wassermann one week ago, the child having reached the age of three months and the blood Wassermann remaining negative. I mean to follow through with a spinal fluid Wassermann, and I am further going to institute arsenical treatment because of the rather unimproved nutritional state of the child. The child made a very nice gain in weight in the first two months with clearing of the pemphigus, then arrived at a standstill, and now is beginning to refuse food. Since she is taking on a dehydrated look, I am advising that the arsenical treatment be used, and we shall see what effect it has on the child generally.

In closing, I want to state that we did not attempt to introduce any new plan of treatment in the present study. We simply selected a small group of cases over which we could exercise sufficient control to have them continue treatment with us. We furnished accessory diets in all cases when necessary in order to properly evaluate effects of treatment and to keep the parents interested in continuing to report at the clinic. We therefore necessarily had to keep our series of cases small, though I am sorry we could not present a much larger series of cases for you, since many cases of congenital syphilis are under observation in our clinics.

PROFESSIONAL ANESTHESIA IN A SMALL COMMUNITY*

By ELDON B. TUCKER, M.D.
Morgantown, West Virginia

Morgantown, West Virginia, is a city with a population of about 18,000. Morgantown is the county seat of Monongalia County, which county has a population of between 50,000 and 55,000 people. The West Virginia University is situated in Morgantown. The chief industry in this county is the mining of coal. Our hospitals have an outside drawing radius which includes 15,000 to 20,000 more people.

Previous to 1922, Morgantown had only one hospital, and this hospital was privately owned, and was a closed hospital. In this hospital, anesthesias were administered by nurses under the supervision of the surgeon who owned the hospital. When the second hospital was opened, one of the first rules adopted stated that all anesthesia in the hospital should be administered by licensed physicians. This old rule has recently been placed in the staff by-laws of the Monongalia General Hospital. It reads as follows:

> Section 6.—Anesthesia shall include the administration of all inhalation, spinal, intravenous, rectal, and nerve blocking anesthesia. It shall include supervision of oxygen therapy. All anesthesia shall be administered by qualified physician anesthetists.

At the City Hospital, which is the privately owned hospital, but which now has an open staff, all anesthesia is administered by physicians. In a recent staff meeting at this hospital it was proposed that a closed staff be made of the anesthesia department.

Not all anesthesia in our community is administered by physicians who are especially qualified to perform this service. The anesthesia administered by the other physicians in this community is largely open drop ether, occasional nitrous oxide, and oxygen for short operations, or as an induction agent, and occasionally spinal anesthesia. Practically all local anesthesia is administered by the operating surgeon. I have had an assistant for the past two years. This assistant has recently given up this work and some effort is being made to resurrect the nurse anesthetist. However, this is not likely to happen in a community which has had medical anesthesia for sixteen years. To return to nurse anesthesia would be a backward step and should not be tolerated by the medical profession.

*Read in Section on Anesthesia, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

GROWTH AND DEVELOPMENT

There has been a steady growth in the number of anesthetics administered as shown by the following table:

Year	Anesthetics	Year	Anesthetics
1924	277	1932	693
1925	284	1933	701
1926	375	1934	808
1927	470	1935	846
1928	540	1936	888
1929	568	1937	1114
1930	756	1938	1540
1931	747		

At first we used open drop ether. Next came nitrous oxide and oxygen, used with and without ether. Later, ethylene was introduced and it is still being used to a limited extent. Spinal anesthesia next had a period of popularity following Pitkin's work on so-called controllable spinal anesthesia. Procaine hydrochloride solutions were used and now procaine and pontocaine are used together and separately, and spinal anesthesia is being employed in selected cases. Cyclopropane and vinyl ether came out at about the same time. Vinyl ether is now used occasionally as an induction agent, for very short operations, or to reinforce nitrous oxide for dental anesthesia. Cyclopropane is filling a very important niche in our anesthesia service. It is used routinely in most major operations, especially on women, with and without ether, ether being added much more frequently than formerly. To date it has been used by us in 1,810 operations. An intravenous barbiturate and tribromethyl alcohol have been used occasionally, but neither has been used extensively.

The use of the newer anesthetic agents has required changes in method of administration. The open and the closed methods of administering gases are used. Endotracheal and intratracheal methods are used occasionally. The rectal and the intravenous technics have been employed. Spinal anesthesia is used in 7 to 10 per cent of cases. A number are given caudal and transacral block. The caudals are administered by the genito-urinary surgeons.

OTHER SERVICES

The anesthesia service is frequently called on for first aid work. We have helped with pa-

tients overcome by various gases, with accident cases in shock, with electrical shock, with patients in convulsions, and with artificial respiration in the newborn. The oxygen therapy naturally belongs under the anesthesia service. Consultations are frequent and occasionally of some value to the surgeon and the patient. We own and operate all of the oxygen therapy apparatus in one of the hospitals. We also own the gas machines which we use and we furnish our own anesthetic agents.

ROUTINE

Operations are routinely scheduled with the anesthetist, usually by the hospital. If conflicts occur as to the hour of operation, they are adjusted at once between the three interested parties: the surgeon, the hospital, and the anesthetist. The hour of many operations has to be changed to suit the convenience of the anesthetist. Patients for a major operation are admitted to the hospital the day preceding the operation. Most of these patients are examined by the anesthetist. If no examination is made by the anesthetist, information is obtained from the head nurse as to age, sex, size, and build of the patient, amount of shock, evidence of hemorrhage, and blood pressure. With this information at hand, knowing the type of operation anticipated and knowing the likes and dislikes of the surgeon as well as his capabilities, the anesthetist then orders the preliminary medication, which is to be given the night and the morning preceding the operation. It is always best for the anesthetist to obtain this information first hand. The selection of the anesthetic agent is practically always made by the anesthetist.

PREMEDICATION

One of the barbiturates, frequently pentobarbital or seconal, is given the night before the operation. Atropine is usually given if either is to be used. We do not care whether the tonsillectomy patient has any preliminary medication. Gas anesthesia is preceded by the use of morphine and hyoscine, usually given one hour before the operation. The dose of morphine is small if cyclopropane is to be used, and it is smaller for the aged and for children, codeine often being substituted for children. If the patient is very nervous, this premedication may be preceded by one or two pentobarbital capsules. Spinal anesthesia cases are usually given pentobarbital grains 1.5 and morphine sulphate grains 1/6 one hour before the operation. Ephedrine or another vasoconstrictor is given a few minutes before the operation. Obstetrical cases are not given morphine near the time of anticipated delivery. Cesarean section patients are given morphine grains 1/6 and hyoscine grains 1/200 to 1/150 at the time the baby is delivered. Morphine may be administered to the spinal anesthesia patient if he becomes very restless during the operation. Morphine may be given to the gas anesthesia patient near the end of the operation if it appears that the patient may react rapidly.

TECHNIC OF ADMINISTRATION

Our technic for general anesthesia is as follows: the patient is examined by the anesthetist, who orders the preliminary medication. General anesthesia for adults and children is induced with gas or ethyl chloride. Usually gas is employed throughout the anesthesia, reinforced frequently with a small amount of ether (10 to 20 c. c.). The pulse is recorded every five minutes. It is counted by the use of a stethoscope attached by adhesive over the precordium. In many operations this method of observation is employed continuously. This is the most accurate way of estimating the effect of the anesthesia upon the heart. Changes in rate and rhythm are noted early. Also respiratory obstruction can be detected by this method. The respiration and blood pressure are recorded every five minutes. Color changes, size of pupil, medication, change of position of table, administration of intravenous fluids, administration of oxygen and other observations are noted on the anesthesia chart. The anesthetist has charge of the administration of fluids and other medication during the operation. He often orders the fluids to be used when the patient is returned to the room.

POSTOPERATIVE FOLLOW-UP

The anesthetist follows up the operative cases with regularity. The patients are examined, suggestions are made, the patients are turned hourly, deep breathing is encouraged. Carbon dioxide is ordered by the anesthetist if the operation was an upper abdominal, if there is much shortness of breath, or elevation of temperature, or diminished breathing over one lung. Fluids, stimulants, position of patient in bed are directed by the anesthetist. The anesthetist is called in emergencies when the surgeon cannot be found. The anesthetist takes an active part in the postoperative follow-up and this is ap-

preciated not only by the patient, but by the surgeon.

TYPES OF ANESTHESIA ACCORDING TO LOCATION OF OPERATION

MOST COMMON OPERATIONS

Head Operations

Mastoidectomy
- Gas induction followed by open drop ether
- Open drop ether from start in small children
- Gas anesthesia

Decompression of skull and brain operations (rare)
- Gas, possibly endo- or intratracheal
- Ether+oxygen
- Tribromethyl alcohol as a basal anesthetic

Paracentesis of tympanum
- Nitrous oxide

Tonsillectomy
- Nitrous oxide or ethyl chloride for induction followed by ether open drop and pump. Head down. Patient turned over after operation
- Nasal tube or airway used on way back to room

Teeth Extraction
- Mostly office cases, no premedication
- Nitrous oxide used. Can add 10 c. c. of vinyl ether if difficult to control patient
- Patient able to go home in short time. Hospital patients are given premedication. Nasal tubes and nasal mask used

Abscesses and lacerations of neck and head
- Gas used

Eye operation
- Local anesthesia, usually administered by the operating surgeon
- Gas, intratracheal
- Intravenous barbiturate
- Ether

Nose
- Local and intravenous barbiturate

Neck

Thyroidectomy
- Cyclopropane
- Nitrous oxide or ethylene if want to give gas under pressure
- Laryngoscope, intratracheal tubes, and tracheotomy tubes kept at hand
- Laryngoscope, tracheal tube used only if obstruction is present or anticipated

Carbuncles of neck
- Nitrous oxide, no explosive gas used
- Intravenous barbiturate

Chest

Thoracotomy
- Local or gas

Thoracoplasty
- Gas, cyclopropane, endo- or intratracheal
- Ethylene or nitrous oxide

Breast
- Cyclopropane
- Nitrous oxide

Abdomen, Upper

Gallbladder
- Few spinal but less than formerly
- Cyclopropane+ether, often an endotracheal tube
- Poor risk, local+gas
- Open drop ether

Perforated peptic ulcer
- Formerly used spinal in most cases. Still a good technic, but now used mostly cyclopropane+ether. Able to place patient in Fowler position earlier following general anesthesia

Pyloroplasty and gastro-enterostomy
- Same as perforated ulcer
- Infants given open drop ether+oxygen for operations for pyloric stenosis or intussusception

Abdomen, Lower

Appendectomy
- Cyclopropane+ether
- Spinal
- Procaine hydrochloride
- Procaine hydrochloride+pontocaine

Pelvic operations on tubes, ovaries, and uterus
- Cyclopropane
- Cyclopropane+ether
- Spinal

Exploratory laparotomy
- Possible intestinal obstruction or colostomy
- Spinal
- Cyclopropane

Accident cases with possible internal hemorrhage
- Cyclopropane
- Cyclopropane+ether

Hernia operations
- Spinal
- Cyclopropane
- Local, given by the surgeon

Suprapubic bladder operation
- Cyclopropane
- Spinal
  - 1, procaine hydrochloride
  - 2, procaine+pontocaine

Prostatectomy
- Cyclopropane
- Spinal
  - 1, procaine
  - 2, pontocaine+procaine
  - 3, pontocaine for transurethral resection

Cystoscopy
- Caudal, given by surgeon

Hemorrhoidectomy
- Spinal, small doses
  - 1, procaine
  - 2, pontocaine
- Cyclopropane

Vaginal operations
- Gas
  - Nitrous oxide
  - Cyclopropane

Circumcisions, hydrocele and scrotal operation
- Gas for adults
- Ether, open drop for small children

Kidney operation
Cyclopropane

Laminectomy and bone grafts to spine
Cyclopropane
Ether, open drop

Extremities

Arms, amputation, plastic operations
Manipulations and drainage of abscess
Cyclopropane
Ethylene
Nitrous oxide

Legs, open and closed reduction of fracture and removal of semilunar cartilage
Spinal
Cyclopropane

Miscellaneous

Manipulation of lower back
Cyclopropane

Some operations about face, nose and eyes
Intravenous barbiturate
Helium has been used occasionally for laryngeal stridor

From June 7, 1938, to October 31, 1939, two thousand anesthetics were administered by us. Five hundred eighty-six anesthetics were administered in our two hospitals by 17 other physicians. The following tables show the anesthetic agents that were employed and also the combination of anesthetic agents used for these 2,000 operations:

ETHER AND ETHER COMBINATIONS

Ether	40
Ether+oxygen	3
Ether+ethyl chloride	281
Ether+nitrous oxide	191
Ether+cyclopropane	367
Ether+cyclopropane+nitrous oxide	9
Ether+cyclopropane+ethylene	1
Ether+vinyl ether	22
Ether+nitrous oxide+vinyl ether	1
Ether+tribromethyl alcohol	1
Ether+cyclopropane+procaine hydrochloride spinal	1
Ether+local+cyclopropane	2
Total	919

CYCLOPROPANE AND CYCLOPROPANE COMBINATIONS

Cyclopropane+oxygen	459
Cyclopropane+ether	367
Cyclopropane+nitrous oxide+ether	9
Cyclopropane+nitrous oxide	14
Cyclopropane+ethylene+ether	1
Cyclopropane+ethylene	2
Cyclopropane+local	7
Cyclopropane+local+ether	2
Cyclopropane+tribromethyl alcohol	2
Cyclopropane+tribromethyl alcohol+ether	1
Cyclopropane+procaine hydrochloride (spinal)	3
Cyclopropane+procaine hydrochloride (spinal)+ether	1
Total	868

NITROUS OXIDE AND NITROUS OXIDE COMBINATIONS

Nitrous oxide+oxygen	317
Nitrous oxide+vinyl ether	6
Nitrous oxide+ethylene	87
Nitrous oxide+ether	191
Nitrous oxide+cyclopropane+ether	9
Nitrous oxide+cyclopropane	14
Nitrous oxide+tribromethyl alcohol	1
Nitrous oxide+vinyl ether+ether	1
Nitrous oxide+procaine hydrochloride (spinal)	1
Total	627

SPINAL ANESTHESIA AGENTS AND COMBINATIONS

Procaine hydrochloride	63
Procaine+pontocaine	40
Procaine+cyclopropane	3
Procaine+nitrous oxide	1
Procaine+cyclopropane+ether	1
Pontocaine	10
Pontocaine+procaine	(40)
Pontocaine+dextrose 10 per cent	7
Procaine with amyloprotamine and strychnine sulfate	20
Total	145

ETHYLENE AND ETHYLENE COMBINATIONS

Ethylene+nitrous oxide	87
Ethylene+cyclopropane+ether	1
Ethylene+cyclopropane	2
Total	90

VINYL ETHER AND VINYL ETHER COMBINATIONS

Vinyl ether	13
Vinyl ether+nitrous oxide	6
Vinyl ether+ether	22
Vinyl ether+nitrous oxide+ether	1
Total	42

LOCAL

Procaine hydrochloride	6
Procaine hydrochloride+cyclopropane	7
Procaine+cyclopropane+ether	2
Procaine, caudal	1
Procaine, caudal transsacral	1
Total	17
Endotracheal	22
Intratracheal	10
Total	32

TRIBROMETHYL ALCOHOL AND TRIBROMETHYL ALCOHOL COMBINATIONS

Tribromethyl alcohol+ether	1
Tribromethyl alcohol+cyclopropane	2
Tribromethyl alcohol+nitrous oxide	1
Tribromethyl alcohol+cyclopropane+ether	1
Intravenous barbiturate	9
Ethyl chloride	11
Ethyl chloride+ether	281

These tables show that in our hands ether is by far the most commonly used anesthetic agent, being used only forty-three times as straight ether, but being used in one combination or another in 45.95 per cent of all administrations. Cyclopropane is second in this tabulation, being used in 43.4 per cent of all operations. Nitrous oxide is third in this tabulation, being used in 31.35 per cent of all operations. Spinal anesthesia is fourth in this tabulation, being used in 7.25 per cent of all operations. Ethylene was used in 4.5 per cent of all operations. Five of the 145 spinal anesthetics required supplemental anesthesia; all five were procaine anesthesia. When pontocaine, pontocaine-procaine and procaine mixture were used, no supplemental anesthesia was required. Ethyl chloride was used in 14.6 per cent of all operations, but practically always for induction of anesthesia, preceding ether anesthesia. Intravenous barbiturate was used for nine operations and the endo- and intratracheal method of administration was employed in thirty-two operations. There were no fatalities on the operating tables and none directly attributable to the anesthesia.

CONCLUSION

We believe we have developed a creditable anesthesia service. A major amount of the anesthesia is administered by qualified physician anesthetists. Newer anesthetic agents can be used successfully in a small community. We believe that our anesthesia service has been a valuable asset to the surgical patient. Our morbidity and mortality have been reduced, and the postoperative follow-up has been life-saving. We believe that anesthesia should be administered by trained professional anesthetists, that the physicians and surgeons of a small community can control the anesthesia of that community, and that they should insist upon the best obtainable anesthetist for their patients.

DISCUSSION (*Abstract*)

Dr. Merrill C. Beck, New Orleans, La.—Dr. Tucker should certainly be complimented on his work in a small community. As you know, in the city we are in now, there are no professional anesthetists. I have spoken to several of the surgeons here and they all say they would like to have one, but none of them will promise to use one if he should come here. So in a city that is much larger and supposedly more advanced than yours, they are very far backward.

Dr. Carl W. Hoeflich, Houston, Texas—Dr. Tucker is practicing anesthesia de luxe, since he is a man who can set the time of the operations.

Dr. J. B. Bogan, Washington, D. C.—Dr. Tucker has done an admirable thing. It undoubtedly has taken a great deal of sacrifice, particularly in the early years of his choosing anesthesia as his specialty.

Dr. T. L. Tidmore, Atlanta, Ga.—I understand that Dr. Tucker uses ether in children for mastoidectomies and similar operations. I wonder why, since children are more prone to form mucus than adults, and since ether certainly stimulates mucus. I wonder whether he has given the gases a thorough trial in those cases. We use the gases down to four to six weeks of age, and we are very well pleased.

Dr. Tucker (closing)—This work has developed gradually in our community. As you can see from the number of anesthetics employed, the size of the community really has not increased in proportion to the increase in the amount of surgery and anesthesia.

I have had some little success in going over the state of West Virginia talking professional anesthesia. For the past three years the State Medical Association has given me permission to put Dr. Ralph Waters and Dr. Henry S. Ruth and Dr. Donald Brace on the state medical program to give papers on anesthesia.

I personally have never had a mastoidectomy in a child that has had a pulmonary complication. With the small child, if we give it a rather large dose of atropine and keep an open airway, and recall the fact that the margin of safety is much greater in ether anesthesia than it is with gas and it is somewhat difficult to hold a gas mask air-tight over the infant's face and to hold the patient's head in a position for the operating surgeon's work, ether is much safer and we have no complications and no reason to change.

UNUSUAL HEAD INJURIES*

WITH A REPORT OF FIVE CASES

By J. M. MEREDITH
University, Virginia

Most physicians are familiar with the usual types of head injury. We wish to present five unusual cases observed in the last three years, together with certain comments on their pathogenesis, diagnosis, differential diagnosis and treatment. They are, in order, (1) delayed extradural hemorrhage; (2) acute subdural subtentorial hematoma; (3) chronic bilateral cerebral subdural hematomata in an infant with apparent congenital hydrocephalus; (4) unilateral massive intraventricular hemorrhage; (5) complete transverse fissure fracture of the middle cranial fossa with a bilateral Bell's palsy.

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*From the Department of Neurological Surgery, University of Virginia Hospital and School of Medicine, Dr. C. C. Coleman, Director.

Case 1.†—Patient admitted three and one-half weeks after injury: mild concussion initially. Headache and diplopia before operation. Linear fracture of the right temporal bone. Large extradural hematoma removed. Leading normal life three years after operation.

A white school boy (Hospital No. 127623), aged 12 years, was admitted to the service of Dr. E. P. Lehman on November 10, 1936.

He was injured twenty-four days before admission when he fell and struck his head. Immediately afterward he became irrational and comatose. Projectile vomiting and severe headache developed. There was great swelling in the right temporal region.

For one week before admission, he had been conscious and rational, but he complained of diplopia.

On admission he was mentally alert, but kept the left eye covered to "keep from seeing double."

There was a bilateral choked disk of several diopters and bilateral weakness of both external recti muscles. All the extremities were moved well.

Dr. Lehman's initial impression was that of a delayed extradural hemorrhage; x-ray examination revealed a linear fracture in the right frontotemporal region.

At operation (Dr. Lehman), in the region of the fracture, the dura was tense and a collection of bloody fluid (100 c. c.) from an old hematoma was encountered extradurally. This contained numerous fragments of organized clot. After its removal, the dural pulsated normally.

Four days later (November 15, 1936) the disks were definitely less elevated although the patient still had diplopia (right external rectus weakness).

One week later he was discharged with no disability except occasional diplopia. The visual acuity was 20/20 in each eye.

Three years after operation, the patient's mother reported that his general condition was excellent. There was no diplopia and vision was excellent.

It is very unusual for a large extradural hemorrhage over a cerebral hemisphere to fail to produce disabling symptoms long before the time that elapsed in this case. The fracture line was not situated in the usual location found associated with an acute clot, but was considerably higher and more anterior; this explains why death or disabling symptoms did not occur much earlier. As emphasized previously by us,[1] when the clot is situated rather high, overlying a cerebral hemisphere, rather than in its usual low-lying position in the middle cranial fossa, compression of the more vital midbrain and brain stem is not so apt to occur (*Fig. 1*). Horrax[2] observed a patient with a similar lesion. McKenzie[3a] reported four cases of extradural hemorrhage that were operated upon from eleven days to three weeks after injury.

†This case is reported with the kind permission of Dr. E. P. Lehman.

Any patient with a linear fracture of the skull vault may develop, as a result of an extradural hemorrhage, signs of increased intracranial pressure requiring operation several weeks after the injury.

Case 2.—Patient admitted directly after injury: apparently moribund (periods of apnea). Marked hypotonia of all extremities. White matter oozing from the right ear: Cerebellar tissue on microscopic examination (?). Large subdural clot overlying right cerebellar hemisphere removed. Death (fifteen days later) from lung abscesses: No residual clot.

A white boy (Hospital No. 148639), aged seventeen years, was admitted May 6, 1939.

He had been rendered unconscious immediately in an automobile accident. He had vomited and there was active bleeding from the right ear, accompanied by the escape of considerable white matter. Respiration was precarious.

The temperature was 98°, pulse 110/M, blood pressure 178 systolic.

He could be aroused slightly; no convulsions had occurred. The extremities were markedly flaccid.

Fifty c. c. of 50 per cent sucrose were administered intravenously by the resident surgeon (Dr. Robert McCullough) with marked improvement in respiration.

Skull x-rays revealed two linear fractures in the right temporo-occipital region.

The material escaping from the right ear resembled cerebellar tissue; microscopic examination was not conclusive. At least an ounce of this material appeared overnight.

The admission impression was: fracture of the right middle fossa extending posteriorly with probable brain stem (medullary) injury; an extra- or subdural hemorrhage was also considered.

The next day (May 7, 1939) he was still unconscious. The temperature was 103° and respiration was very irregular.

Because of the marked hypotonia of the extremities, the escape of cerebellar tissue (?) from the right ear and the peculiar respiratory distress in the absence of clinical evidence of increased intracranial pressure or of localizing signs in the pupils and the extremities, the possibility of a posterior fossa subdural clot was considered. At operation, a large subdural clot was found overlying the right cerebellar hemisphere (Fig. 2). The posterior horn of the right lateral ventricle was also tapped. The clot probably accounted for the precarious respiration and the marked hypotonia of the extremities.

The following day (May 8) slightly active deep tendon reflexes were present for the first time. The right lateral ventricle was tapped occasionally postoperatively. Sucrose was administered intravenously and sulfanilamide was given to prevent meningitis. His condition slowly improved until signs of pulmonary infection developed eight days after operation and he died sixteen days after injury.

A postmortem examination disclosed no residual intracranial clot. Lobular pneumonia, multiple bilateral lung abscesses, and bilateral empyema were found.

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from the brain injury had not pulmonary infection supervened. The lung complications developed in spite of postural drainage and other measures as advocated by Coleman.[4]

Acute subdural subtentorial hematoma has rarely, if ever, been described except in cases of newborn infants examined at necropsy. Schreiber[5] has reported two cases of chronic subdural subtentorial hematoma: (a) a large encysted subdural clot overlying the right cerebellar hemisphere was removed with recovery, (b) a similar clot in a woman with a syndrome suggesting cerebellar tumor; a ventriculogram disclosed an internal hydrocephalus and the patient recovered after removal of the clot.

W. S. Craig[6] found, in 126 newborn infants examined at necropsy, that some of the hemorrhages were mainly subtentorial. In our patient (*Case 2*) the subdural subtentorial clot presumably arose from gross rupture of cortical veins in the right cerebellar hemisphere.

McKenzie[3b] described a case of extradural hemorrhage which extended posteriorly over the cerebellum from its primary location overlying a cerebral hemisphere. We have recently operated upon a patient (November, 1939), who had a large extradural clot overlying the right posterior cerebral hemisphere which arose, not from the middle meningeal artery, but from a tear in the lateral sinus near the sigmoid curve. The hemorrhage was effectively controlled by muscle implants. This particular clot probably extended posteriorly over the right cerebellar hemisphere, as there were no localizing signs whatever except for an equivocal Babinski sign on

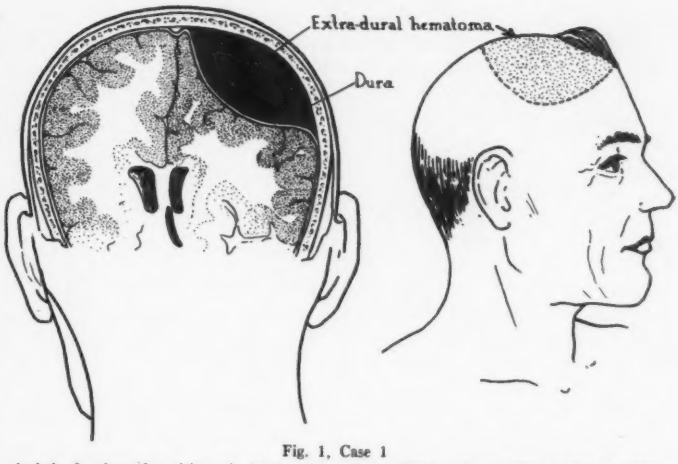

Fig. 1, Case 1

Artist's drawing of position of clot in this patient, showing the relatively high location of the extradural hematoma, resulting in sparing of the midbrain and brain stem. Practically all "late" extradural clots are in a "high" position, not low in the middle cranial fossa, as in the usual acute variety of middle meningeal hemorrhage (by permission of the Editor of the Virginia Medical Monthly).

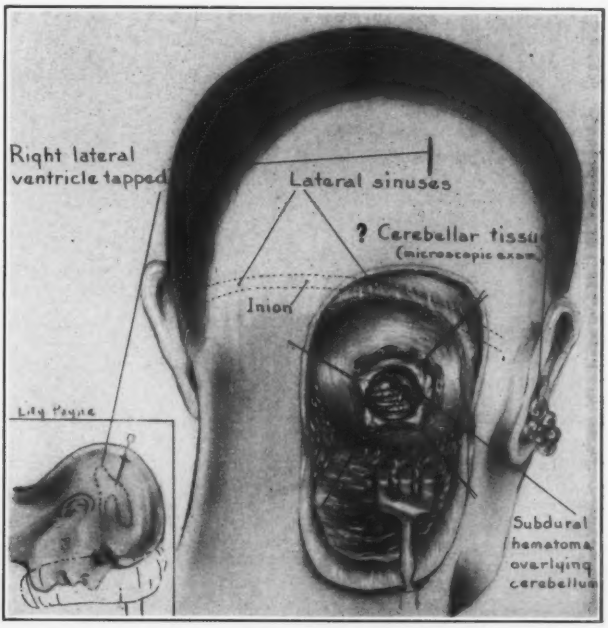

Fig. 2, Case 2

Artist's drawing of acute subdural subtentorial hematoma, removed through an enlarged burr opening over the right cerebellar hemisphere. The cerebellar tissue escaping from the right ear, a suggestive and localizing clinical finding, is clearly shown. Inset shows the right ventricular puncture, repeated several times later in the ward, to combat internal hydrocephalus resulting from post-traumatic edema of the cerebellum.

the left side, together with profuse bleeding from the right ear. Coleman[7] has described a post-traumatic case in which hemorrhage from a lateral sinus almost exsanguinated a patient; the bleeding was also arrested by muscle implants.

The cases cited above, in addition to our own case (2), emphasize the fact that acute post-traumatic clots overlying the cerebellum (sub- or extradural) from posterior extension of a middle meningeal hemorrhage, from tears in the lateral sinus and the tentorium, or from rupture of cortical cerebellar veins, are probably much more common than is usually appreciated. More frequent resort should be had, in post-traumatic cases, to cerebellar exploration, especially if marked hypotonia of the extremities be present, together with (a) shallow, irregular breathing (medullary compression) and (b) absence of localizing signs in the pupils, reflexes and motor power of the extremities in an unconscious patient.

Case 3.—Two months' old child with apparent "congenital hydrocephalus." Bilateral chronic subdural clots disclosed. Ultimate arrest of hydrocephalus with improvement in patient's general condition.

A white girl (Hospital No. 148848), was first examined March 12, 1939.

The child's delivery was difficult and neonatal cyanosis was observed. Enlargement of the head was noticed *at birth*.

When first examined (aged two months), the head was obviously enlarged, its maximum circumference being 40.0 cm. (normal: 37.2 cm.). Two months later, the head measured 46.0 cm. (normal: 38.2 cm.).

She was apathetic and listless and the anterior fontanelle was tense. Skull x-rays showed great thinning of the cranial bones.

Congenital hydrocephalus was considered most likely and the dye test was determined upon.

However, when a lateral angle of the anterior fontanelle was tapped, reddish-orange liquid material was obtained which contained no tumor cells, although 23,800 red blood cells per cu. mm. with 3,000 mg. per cent of protein were present. Undoubtedly the child had chronic bilateral subdural hematomata; the brain was small and the skull had enlarged merely to accommodate the clots (proven to be bilateral at operation).

Two days later (May 17), the clots were removed through superior temporal burr openings (*Fig. 3*), several ounces of reddish-orange fluid being obtained bilaterally; the brain was quite condensed. Thereafter, the fontanelles were retracted; the circumference of the head remained at 46.0 cm., the same as the measurement immediately preceding operation.

Recovery was uneventful except for an attack of severe diarrhea. A follow-up letter (five months after operation), stated that the child was well and had gained several pounds.

Not every infant with gross enlargement of the head and tense fontanelles has congenital hydrocephalus. On the other hand, we have recently seen (1937) another infant whose head was enormously enlarged and who was also thought to have congenital hydrocephalus; the skull enlargement was really due to huge bilateral extradural metastases from an embryonic adrenal tumor, as demonstrated at necropsy. The prognosis in this patient (*Case 3*) is much better than in the average case of well-advanced congenital hydrocephalus.

In tapping a lateral angle of the anterior fon-

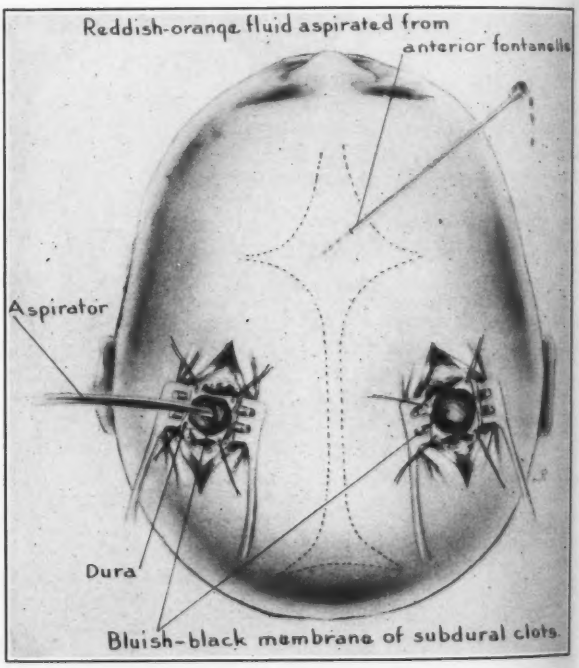

Fig 3, Case 3

Artist's drawing of operative removal of subdural hematomata through bilateral burr openings. The typical outer membrane (similar to that seen in adult cases) immediately beneath the dura is visible: opened on the left side to permit of aspiration of the liquid clot. The pressure of these clots was first verified by obtaining reddish-orange fluid in tapping each lateral angle of the anterior fontanelle. Osteoplastic flaps are rarely required for removal of such clots, in infants or in adults.

tanelle in a congenital hydrocephalic, one ordinarily penetrates through a potential subdural space only, continuing through the thinned out cerebral cortex into the lateral ventricle. In this patient (*Case 3*), the exploring needle encountered a subdural clot immediately on penetrating the fontanelle and dura. Subdural clots in infants are aggravated by the fact that the dura is very adherent to the cranial vault along the suture lines.[8]

When bloody fluid was first obtained in tapping the anterior fontanelle, an intraventricular tumor was considered: possibly a papilloma or a malignant tumor of the choroid plexus, as reported by van Wagenen[9a] who found an intraventricular papilloma in a three months' old infant whose ventricular fluid was xanthochromic.

W. S. Craig[6] stated that it is remarkable that subdural hematomas are not encountered more frequently in infants. In almost 50 per cent of 126 infants studied (at necropsy), gross subdural hemorrhage was present. It is probably the most frequent type of neonatal intracranial hemorrhage. Bleeding may occur *in utero* before labor; this appears likely in Case 3 of this report in which the child's head was enlarged *at birth*. Hemorrhage may possibly occur *in utero* without trauma, due to prolonged bleeding time on the part of the mother, the fetus, or both.

Peet and Kahn[10] described (1932) nine cases of chronic subdural hematoma in infants, primarily diagnosed as congenital hydrocephalus. They noted that percussion over the parietal region in these patients yielded a dull note whereas, in hydrocephalus, a tympanitic note was heard. They had an operative mortality of 55.6 per cent but their patients were operated upon when osteoplastic flaps were generally thought necessary for removal of the clots. Simple burr openings usually suffice, according to Coleman.[11] Ingraham and Heyl[12] have recently (1939) recommended bilateral subdural aspiration through the coronal sutures if they have not as yet united. If the clots are not removed, internal hydrocephalus may result due to the constrictive effect of the clot's membrane about the brain and subsequent interference of absorption of cerebrospinal fluid. Davidoff and Dyke[13] described a curious lesion (four cases) called "relapsing juvenile chronic subdural hematoma." There was invariably a history of trauma in infancy or early childhood together with a second injury which occurred a relatively short time before hospitalization.

In all suspected cases, bilateral burr openings should be made as approximately 20 per cent of the cases are bilateral. Several weeks or months usually elapse after injury or postpartum before alarming symptoms develop. Kaplan[14] reported the case of an eight-year-old child with a chronic subdural hematoma who recovered after operation.

Bucy,[15] in discussing the differential diagnosis of congenital hydrocephalus, mentioned (1) cranial rickets, (2) subdural hematoma and (3) intracranial neoplasm. In subdural clots, the prominence of the parietal bones is usually out of all proportion to the enlargement of the rest of the head. Intracranial tumors usually occur in older children although van Wagenen[9a] described a papilloma in the left lateral ventricle of a three months' old child.

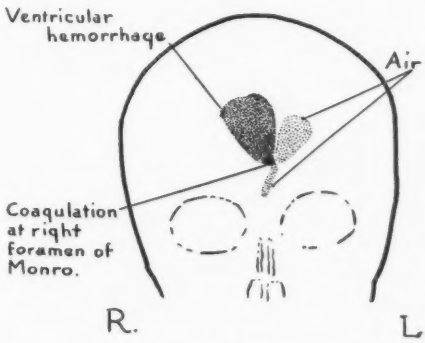

Fig. 4, Case 4

Artist's sketch of the massive right lateral ventricular hemorrhage with spontaneous coagulation at the right foramen of Monro. Air was first injected in the left lateral ventricle (a right cerebral lesion having been presumed, clinically): only the left lateral and the third ventricles filled with air, for obvious reasons. The left lateral ventricular fluid and the spinal fluid contained scarcely any blood; the fluid from the right lateral ventricle contained 1,930,000 red blood cells per cu. mm. (See text).

Case 4.—Nine-year-old girl admitted three days after mild concussion of the brain. Twenty-four hours after injury: severe headache, vomiting and a semiconscious state developed. Lumbar puncture then showed only a few red cells. Five days after injury: massive hemorrhage in right lateral ventricle evacuated. (Left lateral ventricle previously contained practically clear fluid). Subsequent complete recovery.

This patient (Hospital No. 144462) was admitted on November 20, 1938.

Three days before admission she was struck in the face by a swing while playing; she was only slightly dazed.

The next morning, she was in good condition but, later in the day, severe headache developed; she vomited

and became semiconscious. A lumbar puncture was performed: this showed a "hazy fluid, nine white cells per cu. mm. and a few red blood cells." Weakness of the left side developed a few hours thereafter.

When admitted to the hospital, the temperature was 100° (rectally), pulse 64/M, respiration 22/M. She was quite drowsy; the left pupil was larger than the right and the optic disks were hazy.

The left side was completely paralyzed with associated exaggerated reflexes although no ankle clonus or Babinski sign was elicitable. The neck was rather spastic. She had several small port-wine nevi in the skin of the left shoulder.

Skull x-rays were normal. The blood and spinal fluid Wassermann reactions were negative.

The admission diagnosis was "probable right-sided intracranial hemorrhage, with the possibility of a right cerebral tumor to be considered."

Posterior parietal burr openings were made on the night of admission, preliminary to a ventriculogram. The brain pulsated normally.

Two days later, 15 c. c. of air were placed in the left lateral ventricle. Very slightly blood-tinged fluid was first obtained therefrom. The ventriculogram showed air in the left lateral and the third ventricles: both these structures were obviously displaced to the left. No air was seen in the right lateral ventricle. A ventricular needle was then readily placed in the right lateral ventricle and extremely bloody ventricular fluid was encountered (*Fig. 4*). Apparently there had occurred a massive right lateral ventricular hemorrhage with spontaneous coagulation at the right foramen of Monro. The right lateral ventricle was again tapped four hours later and about 20 c. c. of very bloody fluid (containing 1,930,000 red blood cells per cu. mm.) were obtained by gentle aspiration.

Consciousness improved thereafter, although at times she was very stuporous. Strong sedation, including paraldehyde, was required for a few days.

Four days after operation, 15 c. c. of xanthochromic fluid were obtained by lumbar puncture. At this and subsequent punctures, aspiration was necessary as the pressure was zero, presumably due to a partial block of the ventricular system (at the right foramen of Monro) above the point of puncture. Eight days after the removal of the bloody fluid from the right lateral ventricle, she could move the left side well and was almost completely rational. She was discharged fifteen days after the ventricular punctures: the motor power of the legs was then equal bilaterally although slight weakness of the left arm remained. The optic disks were normal and she was entirly rational.

A follow-up report (eleven months after removal of the right ventricular hemorrhage) stated that the patient was in excellent condition.

This patient probably has an angioma or other vascular anomaly in or contiguous to the right lateral ventricle, from which hemorrhage occurred into that ventricle following the slight blow she received. This possibility is suggested by the vascular nevi that are present in the skin of the left shoulder, as emphasized by Cushing and Bailey[16a]. Spontaneous coagulation of the clot must have occurred at the right foramen of Monro as there was scarcely any blood in the left ventricle (the first one tapped) or in the spinal fluid. The spontaneous coagulation of the clot probably had as much to do with the patient's recovery as anything else.

Cushing and Bailey[16b] recorded a case of Dr. R. C. Buckley's of the Yale Medical School that died shortly after hospital admission from the effects of a massive intraventricular hemorrhage: the ventricles were filled with clotted blood from a ruptured angioma venosum in the right occipital lobe. They[16c] also referred to a similar case of Sir Charles Ballance's that had left Jacksonian fits: a venous angioma underlying the arachnoid was found at operation. The patient died five years later and necropsy showed that death was due to a spontaneous hemorrhage. Cushing and Bailey[16d] also described one of their own patients who had a series of six convulsions over a nine years' period after the last of which he had bloody cerebrospinal fluid and papilledema. They concluded that this was almost certainly intraventricular bleeding.

Angiomatous malformations of the brain are usually in the cerebrum,* whereas true blood-vessel tumors, that is, hemangioblastomas, are invariably found in the cerebellum, occasionally as part of Lindau's syndrome, according to Cushing.[17a] Bailey[18a] has described capillary telangiectases of the central nervous system: possibly the patient described above (*Case 4*) has such a lesion. Bailey presented illustrations of two patients with large facial nevi and concomitant cerebral nevi, both of whom had convulsions. Angiomatous lesions usually terminate in intracranial hemorrhage. One of Bailey's patients died after rupture of a venous angioma into the left temporal lobe.[18b] Craig and Lipscomb[19] reported a patient who developed signs suggesting a right cerebral tumor three months after a blow on the head. At operation, a large right intraventricular clot was found which had originated in an angioma in the ventricular wall; this was removed and the patient recovered. They quoted Craig and Adson (1936) who recorded nine cases of intracerebral hemorrhage although the adjacent ventricle was not involved in any case. Most intraventricular hemorrhages are disclosed at necropsy following sudden head-

*We have recently (July 14, 1938) operated upon an eleven-year-old boy who had severe left-sided convulsions for several years associated with unconsciousness. Operation disclosed an enormous venous angioma overlying the right cerebral hemisphere which completely obscured the cerebral cortex. A subtemporal decompression, incorporated in the bone flap, followed by x-ray therapy has resulted in no further convulsions to date.

ache, prostration and death. Gordon[20] described three cases of primary ventricular hemorrhage, all of which resulted fatally. He referred to another previously reported case in which, after drainage of the clot, decided improvement occurred although the patient eventually succumbed.

A bleeding papilloma of the choroid plexus was also considered in our patient (*Case 4*). Van Wagenen[9] collected forty-five cases of ventricular papillomata from the literature and stated that the age incidence was greatest in the first decade of life. He added two additional cases of his own (both in the lateral ventricles). One patient recovered postoperatively; the second was not operated upon and, at necropsy, the tumor was found "seeded" throughout the ventricles.[9b] He recommended x-ray therapy of the tumor (if operated upon in two stages) before operative removel.[9a] Cushing,[17b] in his tabulation of 2023 verified brain tumors, recorded twelve instances of papilloma of the choroid plexus. Nine of these growths were in the posterior fossa and the remaining three were in the lateral ventricles.

Finally, intraventricular hemorrhage may occur spontaneously, as mentioned by Gordon,[20] or it may follow a definite, although slight, traumatic incident (Craig and Lipscomb[19]). W. S. Craig[6] found intraventricular bleeding (occasionally only on one side) in twenty-two newborn infants.

Case 5.—An eighteen-year-old boy was admitted two days after head injury. A cerebrospinal fluid leak from the left ear was present with a complete Bell's palsy and an abducens palsy on the right side. Linear fracture of the left temporal bone (x-ray) extending to the base of the skull. Three days after injury, a complete left Bell's palsy developed for the first time, together with a cerebrospinal leak from the right ear. Eventual complete recovery without operative intervention. Diagnosis: Transverse fissure fracture of middle cranial fossa, producing complete bilateral Bell's palsy and a right abducens palsy within three days of the injury.

This patient (Hospital No. 135085) was admitted October 6, 1937. He was injured two days before admission in an automobile accident at which time he was dazed. Continuous bleeding from the left ear began immediately.

The temperature was 100° (rectally), pulse 64/M, blood pressure 140/80. Blood and probably cerebrospinal fluid were escaping from the left ear; there was a complete Bell's palsy as well as an abducens palsy on the right side.

Skull plates showed a linear fracture of the left temporal bone.

The clinical diagnosis on admission was: concussion of

Fig. 5, Case 5

Photograph of patient about three weeks after injury, at which time the cranial nerve palsies (bilateral complete Bell's palsy and right abducens palsy) were complete. Patient trying to approximate eyelids and to show teeth. Complete inability to perform any seventh nerve function on either side is clearly shown. (Patient also unable to wrinkle forehead on either side by upward gaze).

Fig. 6, Case 5

Photograph of patient about six months after injury, showing almost complete spontaneous recovery from complete bilateral Bell's palsy; right abducens palsy had also disappeared (no diplopia). Patient is able to approximate eyelids satisfactorily on each side (compare with Fig. 5). Other seventh cranial nerve functions were also normal, bilaterally.

the brain with probable complete transverse fissure fracture of the middle cranial fossa (from left to right).

The next day: "the patient now has a complete Bell's palsy on the left side as well, and cerebrospinal fluid is draining from the right ear for the first time."

Four days after the injury the left pupil was larger than the right and the pulse was 50/M but at no time was any concern felt that a clot was developing. Fifty per cent magnesium sulphate (per rectum) relieved the stupor.

The patient slowly improved. On discharge (twenty days after the injury), he was able to hear a watch-tick with the right ear only. The right abducens palsy was slightly improved but the bilateral Bell's palsy was still complete (*Fig. 5*).

Improvement slowly continued and, six months after the injury (April 11, 1938), there was good seventh cranial nerve function on each side (Fig. 6). Two years after the injury (October 20, 1939), the patient's mother reported that his appearance was practically normal.

This remarkable course of events was unique in our experience. The injury to the right seventh cranial nerve and the right abducens was immediate and due to direct contusion of these nerves, whereas the left Bell's palsy, which first developed on the third day after injury, was due to edema rather than to direct nerve injury. If this were true, improvement in the seventh cranial nerve that was first paralyzed (right) should have resulted later than that on the left side; this proved to be the case. Two sequelae were considered: (1) a left-sided extradural or subdural clot, or (2) the possibility that the Bell's palsies (especially that on the right) might not have improved spontaneously: facial-hypoglossal anastomosis would then have been necessary (Coleman[21]).

The diagnosis of transverse fissure fracture of the middle cranial fossa was made, not on the x-ray evidence, but on the clinical course of events as outlined (1937) by Coleman.[7] He stated:

"The limitations of x-ray examination in the demonstration of fracture lines at the base of the skull are well known. The diagnosis must generally depend on bleeding from the cranial orifices, cerebrospinal fluid leaks, suggestive ecchymoses and palsy of the cranial nerves."

SUMMARY

Five instances of unusual head injury are described together with a review of the appropriate literature and emphasis on the remarkable features of each case. These lesions are, in order, (1) delayed extradural (middle meningeal) hemorrhage operated upon successfully three and one-half weeks after the injury, with comment on the reasons for the late appearance of symptoms, (2) acute subdural subtentorial hematoma with discussion of the rather characteristic syndrome associated with such a condition, (3) chronic bilateral supratentorial subdural hematomata in an infant whose appearance greatly suggested congenital hydrocephalus, (4) unilateral massive intraventricular hemorrhage (postoperative recovery) with a discussion of the possible pathogenesis, (5) complete transverse fissure fracture of the middle cranial fossa with a most interesting development of bilateral complete Bell's palsy (spontaneous recovery).

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SURGICAL TREATMENT OF ACOUSTIC NEUROMA*

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In the early Nineteenth Century Cruveilhier[1] gave a fairly accurate description of the clinical findings in acoustic neuroma. The development of localization in the cerebellum during the early part of this century, however, gave a clearer clinical picture of tumors in the posterior fossa. Cushing's[2] memorable medical classic, "Tumors of the Nervus Acusticus" has so clearly outlined the life history of the acoustic tumor that it has been called "Cushing's tumor." Along with this precision in localization came attempts at removal. Needless to say the first attempts were all fatal. The "gynecological finger" enucleation was the procedure of choice, delivering the tumor but producing much hemorrhage and damage to the brain stem and adjacent cranial nerves. Then followed more careful attempts by Sir Victor Horsley, von Eiselsberg and Krause. A survey of this work disclosed a mortality rate of 75 to 85 per cent. This was prohibitive. Cushing, in his inimitable fashion, devised an approach that made possible the exposure of the tumor and an intracapsular enucleation which gave relief for from two to eight years with a mortality rate of 20 per cent. In Cushing's later years he reduced the mortality rate of intracapsular enucleation to 4 per cent. The next important step in the development of treatment of acoustic neuroma came when Dandy advocated the unilateral exposure of the cerebellar cortex after the ipsilateral ventricle had been emptied.[3] The outer third of the cerebellar cortex is then removed and the tumor, growing from and entangled in the cranial nerves, is revealed. The capsule of the tumor is incised and the contents are scooped out. The ninth, tenth and eleventh cranial nerves are identified and separated carefully from the tumor capsule. These nerves are then protected by a piece of cotton. The large artery branching from the vertebral artery and going into the lower pole of the tumor is then clipped and coagulated. This markedly diminishes the blood supply to the tumor. The upper pole of the tumor is freed by gentle traction and careful manipulation. Care should be taken to prevent damage to the fifth cranial nerve, as this produces corneal anesthesia in an eye that cannot be closed by the patient, thus provoking corneal ulceration. The petrosal vein is identified and coagulated. This mobilizes the capsule except from the pons. This separation from the pons is gently and carefully done to prevent damage and, more particularly, hemorrhage. Thus Dandy advocated complete removal in every case and outlined a practical method of doing so. His mortality rate was 20 per cent, which was very favorable.

During the last year a further simplification has been added to this procedure. A small unilateral bone flap extending well up above the lateral sinus with complete and water-tight closure of the posterior fossa is very much to be desired. This greatly simplifies the unilateral approach. It is not necessary to dissect the muscle from the bone flap which is retracted with the muscle attached. The dura is then reflected toward the sinus and there is a beautiful exposure of the posterior fossa with a direct view down the tentorium. (It was also discovered that if the internal auditory canal was not uncapped and thoroughly coagulated the tumor would rapidly recur. This, of course, destroyed the facial nerve, producing a complete peripheral facial palsy.) The dura is then tightly closed, the bone flap is wired in place and the scalp is closed as usual. A light dressing is applied and the patient is allowed out of bed on the fourth or fifth postoperative day. If there has been much damage to the fifth nerve before operation and this persists following operation the eyelids should be sutured together until its function returns. While the patient is still anesthetized, a stomach tube should be passed through which he may be fed. The peripheral facial should be anastomosed to the spinal accessory nerve in the neck about the second week after operation. In the course of six months the function of the facial will be taken over by the spinal accessory and the functional result will be good.

Why should such a radical procedure be undertaken? With it there is a mortality rate of 15 to 20 per cent, while the intracapsular enucleation preserves the function of all the cranial nerves intact and has a mortality rate of only 4 per cent. The answer is that after intracapsular removal, the tumors recur in one to five years and have to be reoperated upon. This reoperation is almost impossible because of adhesions. Recent statistics from the Lahey Clinic[4]

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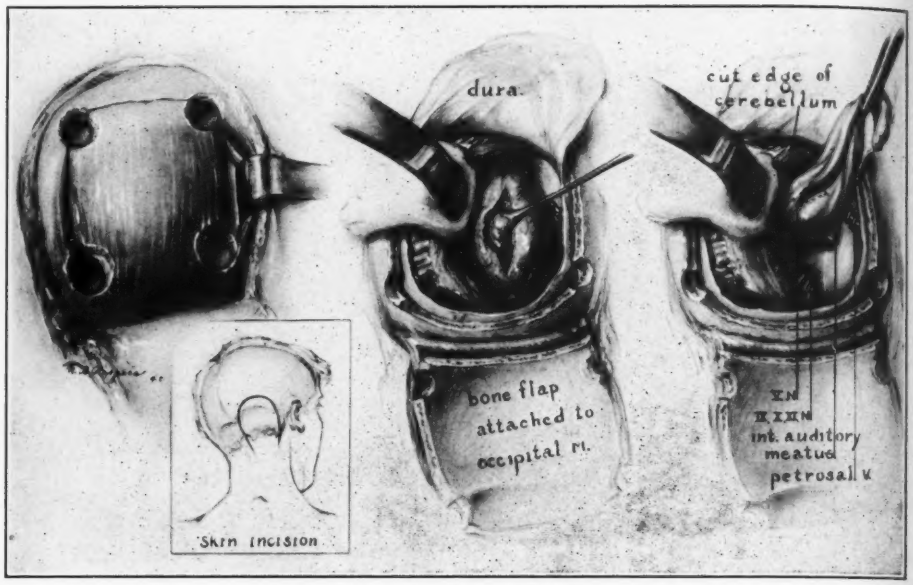

Fig. 1

A unilateral horseshoe incision is made over the right posterior fossa extending up above the lateral sinus down to the muscle. Burr holes are placed as shown and a bone flap elevated attached to muscle and galea. Outer third of the cerebellum is removed and contents of the tumor capsule evacuated. Tumor capsule is gently retracted from the cranial nerves and removed. Internal auditory canal is thoroughly curetted and coagulated.

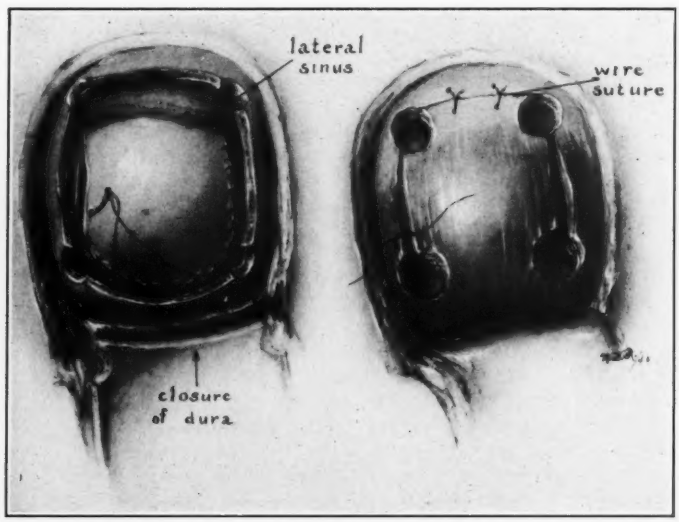

Fig. 2

The dura is closed with interrupted sutures. Bone flap is replaced and wired in place, giving water-tight closure.

show that a total operative mortality for previously unoperated tumors with complete removal was 10.5 per cent. In recurrent cases the mortality was 33.3 per cent. It is very obvious from these figures that complete removal of acoustic neuroma is by far the procedure of choice. A more conservative attitude is justified, however, if, excluding the tumor, the ultimate life of the patient is thought to be short.

CASE REPORT

F. K., a white mill worker, aged 50 years, was admitted to the University Hospital with a diagnosis of acoustic neuroma on December 29, 1939. This patient was referred by Dr. R. L. Gibson, of Columbus, Georgia.

The history dates back 18 months, when the patient noticed that he was getting deaf in the right ear. With this deafness he also noticed a ringing. Following this, several months later, severe nausea, vomiting and headache developed. These symptoms improved under rest and treatment. He developed a falling to the right when walking, and during the last several months before admission he was confined to bed because of inability to walk. While in bed he developed a nasal, bulbar speech with difficulty in swallowing. His vision also became impaired to such an extent that he was unable to read.

The general physical examination disclosed a well developed male in apparent distress, suffering from severe headache and a clouding of consciousness. Heart and lungs were normal. His blood pressure was 110/70, pulse 88, and respiration 18. On neurological examination he presented a mental confusion characteristic of intracranial pressure. He was dehydrated and somewhat weak. Examination of the cranial nerves disclosed choked discs of 3 to 5 diopters in both eyes with many hemorrhages. The visual field showed enlargement of the blind spot and general constriction of the field. There was a weakness of the right sixth nerve. The third was intact. There was a loss of sensation over the entire distribution of the fifth nerve. This was most marked in the first division with absolute loss of corneal sensation. There was loss of motor power in the right jaw. There was a peripheral facial weakness on the right. This was not so marked as one would expect, which shows the extreme elasticity of the seventh nerve. There was no loss of taste. There was a marked lateral nystagmus, more marked to the right but present bilaterally. Hearing was gone in the right ear, as was the ringing. Vestibular tests disclosed no function in the right labyrinth (both caloric and rotation). There was impairment of the ninth nerve on the right. The gag reflex was absent. Hoarseness was marked and the vocal cords on the right were more relaxed than on the left, indicating involvement of the right vagus nerve. The eleventh and twelfth were not affected.

From the history the first nerve affected was the eighth; consequently a positive diagnosis of eighth nerve tumor could be made when we took into consideration that he was exactly in the age group in which eighth nerve tumors usually occur. The involvement of the second and sixth nerves pointed to generalized intracranial pressure. Examination of the sensory system disclosed a loss of pain and temperature and some touch over the shoulder and right arm. The motor system presented marked asynergia in the entire right side. The left side was normal. There was no atrophy and no abnormal movements were present. There was a weakness of the right leg. The deep reflexes in the right leg were more active than in the left leg, and there was a right Babinski with absence of right abdominal reflexes. The sympathetic and endocrine systems were normal. Thus we found involvement of the lateral recess of the pontine region with loss of temperature and pain in the arm, neck and shoulder (lateral lemniscus). The increase in reflexes in the right side with weakness indicated involvement of the corticospinal tract contralaterally to transmitted pressure of the cerebral peduncle against the incisura of the tentorium. There was asynergia due to direct pressure against the inferior arm of the cerebellum and also to direct pressure against the cerebellum which is ipsilateral. Because of marked increase in intracranial pressure it is not wise to do lumbar punctures on these cases; consequently none was done. An x-ray was taken which showed an erosion of the internal auditory meatus, making the diagnosis of an acoustic neuroma certain.

On January 3, 1940, a unilateral osteoplastic craniotomy was done on the right side under intratracheal anesthesia. The outer edge of the cerebellum was excised and an intracapsular enucleation of the tumor was done. The capsule was separated from the ninth, tenth and eleventh nerves, as well as the fifth, to which it was firmly adherent. The capsule was then removed. The upper tip of the internal auditory canal was chiseled away and the remnants of the canal thoroughly coagulated to prevent recurrence of the tumor. The patient made an uneventful recovery. He wished to return home before having the spinal accessory sutured to the peripheral facial; therefore the lids of the right eye were sutured together and he was allowed to return to Columbus. Unfortunately the lids separated after his return home and he came back to the hospital with a corneal ulcer. This was treated successfully and the spinal accessory was sutured to the facial one month after the first operation. He is walking about and his condition is good except for the persistent hypesthesia in the first division of the fifth nerve and the peripheral facial, which will be corrected in six months. Some sensation was present in the cornea at the time of his second discharge. The simplicity of total removal of far advanced acoustic neuroma by unilateral craniotomy should be stressed.

SUMMARY

(1) Progress in the development of surgery of the acoustic neuroma has been presented.

(2) A typical case has been selected and presented to demonstrate the neurologic findings and diagnosis.

(3) A new and more satisfactory approach to the posterior fossa and the cerebellar pontine angle has been illustrated.

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CEREBRAL COMPLICATIONS IN SICKLE CELL ANEMIA*

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A purpose of this presentation is to place on record an unusual case of sickle cell anemia with striking multiple cerebral lesions. In the medical literature, now comprising well over one hundred contributions, there are only twelve previously reported cases with assured pathologic involvement of the brain. However, none of these few has presented such extensive neurologic features as our patient. The active cases of sickle cell anemia are comparatively infrequent. The latent sickle cell trait, "sicklemia," is fairly common in persons with negro blood.

Herrick,[1] in 1910, reported the first case establishing the definite clinical entity of sickle cell anemia. A second one in 1911 by Washburn[2] and the third in 1915 by Cook[3] were recorded. The name sickle cell anemia seemingly was applied first by Mason[4] in 1922. Irregular shapes for the erythrocytes had been recognized some years earlier by Hayem,[5] Dresbach[6] and the Sargents.[7] The Sargent[7] brothers and Langeron[8] described "demilune" red corpuscles in rats and guinea pigs, and in malaria and plumbism. After 1922 the scientific literature accumulated more rapidly.

HEREDITY

Numerous studies suggest that the latent sicklemia and the active sickle cell anemia are confined essentially to the colored race. The few supposedly white patients so afflicted are reported by Archibald,[9] Lawrence,[10] Cooley and Lee,[11] Sights and Simon,[12] Rosenfeld and Pincus,[13] Clarke,[14] Cooke and Mack,[15] Wallace and Killingsworth,[16] Haden and Evans,[17] Johnson and Townsend,[18] and Weiner.[19] Most of the few contrary cases found in the literature are to be questioned. They issue almost entirely from Mediterranean races, not far from Africa. The two cases reported by Sights and Simon[12] and Cooke and Mack[15] may be exceptions. Haden and Evans[17] admit a possible doubt about the racial factor in their two cases (sisters). Wallace and Killingsworth[16] report the latent sicklemia in a Texas Mexican family, including the mother and two sisters whose ancestors were possibly Aztec. In these very few it must be considered that a throw back through a number of generations may make it exceedingly difficult to be assured that there is not even a slight admixture of colored blood. Anthropologic studies teach us that to boast of absolute racial purity is quite hazardous. The hereditary features have been indicated by Sydenstricker, Mulherin and Houseal,[20] Cooley and Lee,[11] Huck and Bigalow,[21] Vaughan,[22] and Graham and McCarty.[23]

All critical analyses of sicklemia and sickle cell anemia demonstrate that the interesting phenomena have distinct hereditary characteristics. Resorting to the Mendelian law, we find the dominant characteristics. For the negro race in the United States we may expect to find sicklemia in about 5 to 8 per cent of all cases investigated. Most of the literature emanates from North America. Only one article can be credited to Africa, namely, by Russell and Taylor.[24] Relative to this matter an interesting opportunity may be offered for comparative blood studies in the various African tribes.

Probably sickle cell anemia always develops on a previously existing sicklemia. The modus operandi of the hemolytic changes is not adequately understood. Possibly when there is more knowledge relative to these phenomena an avenue of approach will be at hand to develop a preventive in the latent period or a cure for the active sickle cell anemia. Regressions and repeated recurrences are not uncommon in the customary long course of the illness.

SYMPTOMATOLOGY

The diagnosis has been made usually between the years of 3 and 30, but possibly no age is exempt. Look for the trouble almost exclusively in the negroid race. A certain habitus has been described, but no single one is characteristic. Frequently the patient presents a pale, languid state, developmental defects and fatigues much too readily. Cranial abnormalities, including "Turmschadel," have been described. Although he may be smaller than normal, yet the tall type may be affected. Where the disease starts in early childhood, as often happens, developmental abnormalities are common. Pallor and greenish-yellow sclerae usually are striking. We are impressed promptly by the anemia. Abdominal pains, often severe and suggesting various surgical diseases, have been recorded often. In

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*All illustrations are taken from 16 mm. colored motion picture films.

fact, the abdomen has been opened by surgeons too frequently only to not find a suspected pathologic gallbladder, appendix, or other visceral lesions. There are frequent complaints of various types of pain in the lower extremities, sometimes suggesting rheumatic states. Indolent leg ulcers are common, usually below the knees or just above the ankles. An enlarged spleen, especially in the early stages, may be detected. After a few years, atrophy frequently takes place, occasionally only a sclerotic trace of the organ being found at the autopsy or operation.

The blood picture is always interesting and of great diagnostic value. The anemia and accompanying jaundice, especially as observed in the sclerae, are striking. Care has to be exercised in differentiating this disease from chronic hemolytic icterus, erythroblastic and pernicious anemia. The erythrocytes are sickled, oat-shaped, elliptical or presenting a multiplicity of bizarre forms. Many red cells are larger or smaller than normal. Some long, fine filaments may project. Nucleated reds may be numerous in the vascular system as well as the bone marrow and spleen. Poikilocytosis may be a part of the blood picture. The erythrocyte count frequently ranges from 1,000,000 to 3,000,000 per cu. mm. There is a corresponding reduction in the hemoglobin with a normal color index. The platelets are normal. The icteric index often is high. The clotting and bleeding time are normal. While you may see at once these various changes in a fresh wet smear, yet other methods at times are required to demonstrate the abnormal reds. If a moist specimen is sealed an apparently negative sickling may become positive in 2 to 24 hours. Frequently 50 per cent or more of all the erythrocytes show the sickling form where resort is had to this artificial anoxemia. This phenomenon may be reversed by an increase of oxygen and decrease of carbon dioxide. Changes in the red cells also are encountered in the spleen, liver and regularly in the bone marrow which becomes intensely red or grayish red. We can summarize that for some unknown reason there is an excessive destruction of the red blood corpuscles. Associated with this or immediately following comes a great demand on the hemopoietic organs to replace the huge loss. Accordingly we see coming from the overworked red bone marrow reticulocytes, nucleated reds and other premature types. With the destruction of the erythrocytes, there appears a yellowish discoloration in the sclerae and deposits of cellular debris, especially iron pigments in the spleen, liver and other large organs.

These blood changes are commented upon by many research workers. However, similar changes also have been noted in chronic hemolytic icterus, and erythrocytic anemia. Dresbach[6] in 1904, Herrick[1] in 1910, Washburn[2] in 1911, and Emmel[25] in 1917 described pathological erythrocytes as related to sicklemia and sickle cell anemia. Valuable contributions to the hematology have been furnished by Diggs and Bibb,[26] Sydenstricker,[27 28] Huck,[29] Auer,[30] Mason,[4] Steinberg,[31] Scriver and Waugh,[32] and Campbell.[33] Smith[34] noted sickling in Mexican and Persian deer.

Here it may be interesting to note that skull changes similar to those found in sickle cell anemia have been observed in the mummies from the ancient Peruvians and Mayans of many centuries ago. Your attention may be called to the osteoporosis frequently encountered in this disease, at times only determined by x-ray examinations. The outer table of the skull may be completely obliterated and the cranial vertex frequently is increased in thickness, at times measuring as much as 2 cm. The frontal and parietal bones especially are involved. The striking "hair-on-end" manifestation of the cranial vertex frequently demonstrated in roentgenograms may be of much diagnostic value. The almost vertically placed fine bony spicules seem to spring from the outer table of skull. Possibly the hyperplasia of the diploe is responsible for this curious x-ray finding. Thus the processes of degeneration and repair are going on at the same time or in successions in the flat as well as long bones. The bones of the cranial base and face are mostly normal. Decalcification has been demonstrated in the long bones. Good accounts of skull and long bone changes may be found in the writings of Diggs, Pulliam and King,[35] Le Wald,[36] Caffey[37] and Brandau.[38] Suggestive similarities in the bones of the ancient Mayans and Peruvians are recorded by Moore[39] and Harden.[40]

PATHOLOGY

In the pathology of sicklemia and sickle cell anemia, our attention in particular is focused on the hemopoietic and hemolytic elements or organs. Seemingly histologic changes in the erythrocytes are of great importance for the diagnosis and pathology. Careful studies of them alone usually will assure a recognition of the disease. The essential blood changes have been described

above. Many of the pathological tissue changes are secondary to the blood defects. Your attention might be called especially to the tendencies for ulcerations in the lower extremities, abdominal crises, heart symptoms, and even the brain lesions which concern this presentation primarily. Thromboses and hemorrhagic infarcts occur with great frequency in many organs. These are responsible for the leg ulcers. Especially are they encountered, and with many repetitions during months or years, in the spleen, abdominal and other organs. I believe this will account for complicating pathology in the very few cases reported in the literature where the brain has become involved. Then with the repetition of these vascular changes and a long-time deposit of blood debris, there occurs the pigmentation in the tissues and fibroses, including siderofibrosis. The spleen usually is enlarged in the early stages, frequently to a great degree, and especially in children. A long time later following many pathological bombardments the spleen may atrophy considerably, even to the extent where only a small fibrotic mass remains. There is one reported case in the literature where the spleen was not found at an abdominal surgical operation for splenectomy on account of the complete atrophy. The spleen has been suspected as a cause of the disease, and with hereditary tendencies. Two extremes in size are illuminating. Ching and Diggs[41] found at death of a child a spleen weighing only 10.5 grams with an abundance of sickle cells in the pulp. Sydenstricker, Mulherin and Houseal[20] discovered at the autopsy on an 8-year-old negro a spleen with a weight of 7.9 grams. Bridgers[42] reports a 4-year-old negress with an originally markedly enlarged spleen which degenerated to a fibrotic mass and finally presented a postmortem weight of only 1.5 grams. The other extreme is illustrated by an autopsied organ weighing 621 grams, according to Landon and Lyman.[43] The cranial and long bone changes, especially in the osteal marrow, might be a result of excessive demands to replace the impoverished erythrocytes.

Although the hemopoietic organs have been searched intensively for the cause of the disease, the exact modus operandi up to this date is not clear.

DIAGNOSIS

It may be interesting to consider that in a differential diagnosis we have but a few hemolytic or destructive blood diseases seriously to be considered. Pernicious anemia may be ruled out readily by the high color index, gastric changes and lastly by the therapeutic liver test. Familial hemolytic icterus and erythroblastic anemia are more difficult to differentiate. Many of the diagnostic symptoms, including sidero-fibrotic lesions, thromboses, leg ulcers, somewhat similar blood pictures and the characteristic pathology of the calvarium may be encountered in them.

PROGNOSIS

The disease is essentially decidedly chronic. An exitus in early life is usually the final outcome. Children, so often afflicted, seldom reach 30 years of age. Death may occur from many complications such as pulmonary troubles, especially tuberculosis, various infections, abdominal and cerebral thromboses. There is a general susceptibility and reduced resistence to the various terminal diseases. Seldom does the erythrocytic count reach normal where the reduction has approached about 2,000,000. Pregnancies, very poorly tolerated, are contraindicated according to Page and Silton[44] and Lewis.[45]

TREATMENT

Only a sad chapter may be written regarding the treatment up to date. Essentially is our attack confined to preventing the many possible infections or traumatic lesions. Symptomatic treatment naturally is indicated for any of the secondary lesions so frequently encountered. Liver therapy, iron, arsenicals and transfusions may be of some value, though never specific. Torrance and Schnabel alone write in favor of potassium sulphocyanate. They report a clinical improvement, but not for the blood picture at the end of one month of treatment. You may be attracted to several reports on splenectomy. A few mild temporary improvements have been reported, but the long-time final results have been useless for most of the operated patients. Writings in favor of the removal of the spleen come from Hahn and Gillespie,[46] Bothe,[47] Haden,[17] Grob[48] and Yater and Mollari.[49] Contrasting negative results are recorded by Bosselman and Kraines,[50] Cooley and Lee,[11] Ching and Diggs,[41] Yater and Mollari,[49] Bell *et al.*,[51] Leivy and Schnabel,[52] Stewart,[53] and Landon and Lyman.[43] The poor final outcome is in striking contrast to hemolytic jaundice in which there is a very high percentage of restorations following splenectomy. As a corollary your attention might be called to a more or less complete de-

struction of the spleen in many long-standing cases, only to observe always the continued retrogression, at times broken with improvements, eventually terminating in death. Are we going to heed this natural experimental data?

CASE REPORT

R. J., a 34-year-old male negro, was admitted to the Kansas City General Hospital No. 2 (colored), on April 26, 1938.

He had been a good reliable chauffeur for a number of years with excellent habits. The rather abrupt apparent onset of his illness was indicated with an early severe paralysis of the right side and a striking defect of speech. The employer of the patient stated that apparently he had been in perfect health up to June 15, 1937. At this time, after a motor trip, he complained of severe abdominal cramps, nausea, vomiting and headache. On the following morning he was paralyzed on the right side. He was admitted first to another hospital on June 20, 1937, where their records indicated nausea, vomiting, diarrhea and some excruciating occipital pains which reached the left cervical and mastoid region after four days. He improved at this hospital and was discharged on July 14. On August 28, 1937, he was returned with similar symptoms. During these first two hospitalizations the erythrocyte count was reported from 4,140,000 to 4,930,000. The leukocyte count once was 16,400 and another time normal. The hemoglobin was 85 per cent. His temperature for two weeks ranged from 99 to 102 degrees.

No positive differential diagnosis was made during the first two hospital admissions. The attending man and consultants (one a neurosurgeon) considered cerebrospinal syphilis, brain tumor and sickle cell anemia.

A meager family history records no similar trouble or sicklemia. As far as the patient knows, no sickle cells had been found previously in his blood. In 1923 he took "some shots" for symptoms that were not marked, possibly for suspected lues. The patient denies any primary syphilitic lesions. We believe that he never had syphilis.

Examinations.—The patient is a well-developed, large male negro, about six feet tall. His genitalia are normal. No endocrine disturbance is noted. The anemia is quite evident on inspection with a striking greenish-yellow color of both sclerae. His blood pressure was originally 110 over 70, and has never been much higher. No cardiac or pulmonary troubles were noted. Possibly the liver was a little enlarged. The spleen was not felt. There is an almost complete right motor hemiplegia. He could not move either fingers or wrist. Slight shoulder movements are present. Some feeble voluntary movements in the right lower extremity are noted. The patient can move about only with a crutch. The deep reflexes on the right side are greatly increased with a well sustained ankle and patellar clonus. A strongly positive extensor toe sign is obtained on the right side to the several tests. The left is negative. He has a positive right Hoffman and negative left. All deep reflexes are brisk. A few scars are present on the lower extremities below the knee, suggesting past ulcers. His senses of smell, taste and hearing apparently are about normal. Vision seems to be good. The left eye as reported by the oculist shows some restriction for the field of vision for all colors. A left homonymous hemianopsia is present. No abnormalities are seen at the optic nerve heads. A complete ptosis of the left upper eyelid is present. In looking straight ahead the left eyeball is turned outward. The pupil is dilated. The second, third and fourth cranial nerves are apparently normal in the right eye. In the left there is a complete paralysis of the third and fourth cranial nerves, but the sixth is intact. There is a marked right seventh motor palsy. The motor fifth is normal on both sides, but a mild right sensory impairment is evident. The twelfth cranial nerve shows a little weakness on the left, the tongue deviating to that side when protruded. The entire right side of the body supplied by the spinal nerves presents a moderate anesthesia and analgesia. This also involves the fifth cranial nerve area on the same side.

The mentality of the patient shows little or no impairment. He is quite clear on every topic when he can make himself understood. However, his striking motor aphasia makes for us a rather poor neurological witness. His speech is improving, but continues quite limited. When the wrong word is spoken, which happens so frequently, he promptly recognizes the error, but usually cannot correct it.

During a year and a half of observation in the hospital, the patient has repeatedly shown an erythrocyte count of only about one-half the normal, ranging at different times from 1,970,000 to 3,100,000. The hemoglobin has been correspondingly low, 45 to 65 per cent. The white cell count has usually been normal, on one occasion going to 10,800 and on another 10,250. A few sickle, oat-shaped and various other abnormal red cells can be seen at any time when a specimen of blood is observed. However, more than 50 per cent of the cells become abnormal in shape when a fresh, sealed specimen is observed after a few hours to one day. The icteric index was as high as 30 at one time. Reticulated cells at the same time were 6.25 per cent. The fragility test did not show any marked change. Blood chemistry had always been negative. Wassermann and Kahn on the blood and spinal fluid have repeatedly been negative. Several tests on the spinal fluid have shown neg-

Fig. 1, Case R. J.
Face illustrating right facial and left third cranial motor nerve palsies.

ative findings, with no appreciable increase in pressure, a negative globulin and all zeros in the goldsol. Repeated urine and sputum tests have always shown normal findings.

A number of roentgenograms were made by Dr. Chas. R. Humbert. The parietal skull shows much thickening, with the outer table very feebly outlined. The "hair-on-end" phenomenon is striking, especially over the parietal bones. No pathology is noted for the sella or basilar region of the skull or face. The long bones of the arms and legs bear evidence of diffused decalcification.

A toe ulcer developed while in the hospital which was very slow in repairing. During July, 1939, with a very slight trauma there occurred a fracture of the right tibia, the x-ray showing it at the intertrochanteric line. The shaft and upper fragment are at right angles and no attempt to repair can be seen. He also has had one attack of bronchitis which was slow to recover.

With all of these findings there was no trouble in making a certain diagnosis of sickle cell anemia. Unfortunately we have no opportunity to check up on any of the relatives for the sicklemia trait. Treatment has been largely symptomatic, using iron, arsenic and liver. His progress has been variable, with improvements and retrogressions.

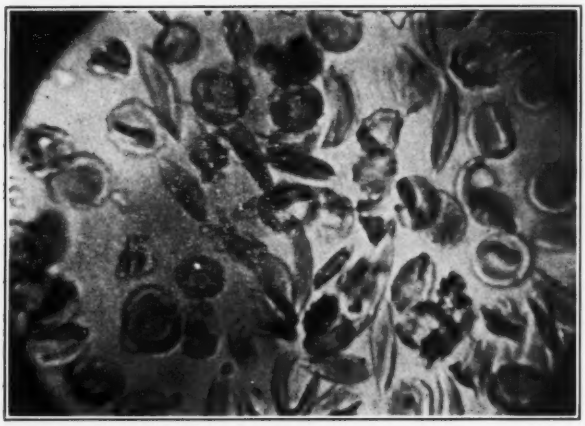

Fig. 2, Case R. J.
Photomicrograph of twelve-hour wet blood specimen. Sickling and many other red corpuscle deformities.

Fig. 3, Case R. J.
Skull. Frontal bone. Much increased thickness and fusion of tables. "Hair on end" with verticle spicules striking.

DISCUSSION

The first case of sickle cell anemia complicated with intracranial pathology was reported by Cook[54] in 1930. Clinically his 7-year-old male negro patient presented a nystagmus, hemorrhages in the right fundus and a flaccid palsy with no deep reflexes obtainable. The spinal fluid had increased pressure, a four plus globulin, a white cell count of 130, and an erythrocyte count of 1,400 with sickling of many. The autopsy revealed a right subarachnoid hemorrhage and cerebral softening besides a thymolymphadenopathy, marked anemia, striking bone marrow hyperplasia and a shriveled spleen weighing 20 grams. Arena,[55] in 1935, placed on record a negro boy, aged 6, with sickle cell anemia having a moderate flaccid weakness of right leg and arm with increased deep reflexes, a positive Babinski, a mild right facial palsy, and bloody spinal fluid containing many sickled erythrocytes. This same writer,[56] in 1939, places on record four additional cases of sickle cell anemia in children with various complicating plegias; and in a private communication states that a total of eight cases with brain involvement have come to their notice. Their pathologist, Dr. Bridgers,[42] reports on a complete autopsy for one of the children revealing occlusions of large subarachnoid cerebral arteries. His second postmortem details a 62-year-old negress with typical abdominal, back and leg pains and some mild neurological positive signs, all with a recent onset. Sickled erythrocytes were found

in the various organs. Minute cerebral hemorrhages with hemorrhagic infarcts in especially the brain as well as spleen, heart and lungs were noted. The autopsied case of Baird's[57] 42-year-old negro demonstrated multiple infarcts in the spleen, heart, lungs and kidneys. There were clinical signs in the brain which was not removed. Proven syphilis raises a complicating question. Yater and Hansmann,[58] in 1936, reported on a negro, aged 38, dying with sickle cell anemia. The autopsy demonstrated a one centimeter softened area in the left parietal cortex, a shrunken choroid plexus, cord petichae, and a small fiberous placque over the posterior lumbar segments. Many small thromboses were found in the lungs. Kampmeier[59] placed on record in 1936 a case of sickle cell anemia with a right-side paralysis, involving the seventh cranial nerve, and a ptosis on the same side. Bloody spinal fluid was obtained and the erythrocytes showed sickling in four hours. Ford,[60] in 1937, cites an intracranial postmortem on an 18-months-old negro child with a thrombosis of the superior longitudinal sinus, subarachnoidean hemorrhages and cerebral areas with hemorrhagic softenings. Bosselman and Kraines,[52] in 1937, described the complication of aphasia in a 13-year-old negro, also showing mental deficiencies. They cite an unreported autopsied case from a Chicago hospital with chronic leptomeningitis and bloody extravasations in cerebral tissues. Josey,[61] this year, reports cerebral thromboses in an 8-year-old negro boy, covering a five-year period of observation, with a variable aphasia and changing palsies.

SUMMARY

(1) An unusual case of sickle cell anemia in an adult negro with a complete hemiplegia, a persistent motor aphasia and several cranial nerve palsies is reported herewith. The blood pathology and roentgenograms of the calvarium demonstrate conclusively the diagnosis.

(2) Comparatively few other cases with cerebrospinal complications are reported in the literature, none having as extensive a clinical pathology in the brain.

(3) The multiple cerebral lesions may be attributed to several thromboses, one quite extensive in and around the left internal capsule, producing a severe permanent right hemiplegia with motor aphasia. Some additional accompanying hemorrhages, mostly small, may be suspected.

(4) It is anticipated that an increased number of cerebrospinal complications may be noted in the future with more clinical alertness on the part of diagnosticians.

(5) The present day prognosis for a patient suffering from the active sickle cell anemia is a sad one. It is not presumptuous to look to the future for some specific treatment comparable with that which has been discovered for pernicious anemia or hemolytic jaundice.

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DISCUSSION (*Abstract*)

Dr. James G. Hughes, Memphis, Tenn.—The most striking thing about Dr. Skoog's report is the fact that he has recorded for the first time multiple cranial nerve palsies as a complication of sickle cell anemia. There have been several reports of hemiplegia and aphasia in sickle cell anemia patients, but no previous cases of multiple cranial nerve palsies.

At the John Gaston Hospital, Dr. Diggs and I have observed five cases of cerebral complications in sickle cell anemia out of a total group of about fifty sickle cell anemia patients. The clinical data concerning these five cases and postmortem findings of two of them will form the basis of a subsequent report.

Twenty-three reports of cerebral complications in sickle cell anemia have been found in the literature. The commonest symptoms in the order of frequency have been hemiplegia, stupor and coma, convulsions, and severe headaches. There have been six cases of aphasia. Dr. Skoog's is the seventh. Curiously enough spinal fluid findings have been characterized by great variability. In seven spinal fluid examinations, including two of our own, grossly bloody fluid has been reported twice, xanthochromic fluid once, and grossly normal fluid four times. Increased pressure and slightly increased albumin may occur in fluid which appears grossly normal. The reported instances of examinations are too few to draw any conclusions. The fluid may be normal or it may be quite pathologic.

The prognosis of cerebral complications in the reported cases of sickle cell anemia is very poor. Over fifty per cent of the cases have died after a variable, usually short period following the onset of symptoms. As a rule, they die within a few weeks. Those who have survived may be left crippled, like the case reported by Dr. Skoog, or if recovery does occur they may fall prey to subsequent exacerbations. The case Kampmeier reported is a typical case of subsequent exacerbations.

None of the various types of treatment which have been tried has been of any avail.

The cerebral pathology of sickle cell anemia is chiefly due to thrombosis of cerebral vessels, particularly those supplying the cortex. Hemorrhages, infarction and resultant atrophy may occur with variable neurologic phenomena.

Dr. William Nelson, St. Louis, Mo.—I should like to make a few remarks about the physiology and the embryology of the blood and link it up, if I may, with some of the manifestations or some of the physical findings that are present in this disease.

Lack of oxygenation of tissues is not always dependent upon asphyxia from a cutting off of the blood supply or of the channels through which the blood circulates to carry oxygen. It may be a much more primary thing than that resident within hemopoietic tissues. It may be due to lack of evolution of the blood forming structures.

In this disease we go back to the liver and to the spleen. Embryologically, the red cells come chiefly, I believe it is the admission of most hematologists, from the liver and spleen. Since that is true, and since here is largely a survival, in spite of certain obstacles or impediments that are created within the individual, we could liken this to what Gowers has said about some of the illnesses which are subject to an abiotrophy, if you will, or biological deficiency in the hemopoietic tissues. However, we cannot attribute them all to the same cause, because we have always added secondary mechanical influences to which the organism is subjected.

It is not an inflammatory sort of change which takes

place in the vessel, but actually a mechanical change due to a failure in the nutrition of the tissue fundamentally dependent upon lack of hemopoietic activities or principles, in the organs that produce the blood.

We need to think beyond the clinical symptoms and pathologic findings at the time of examination.

Dr. Skoog mentioned the deficiencies in the flat bones. In the flat bones we have red marrow early, and it is from the red marrow that the red blood cells come. It is a reversion, if you will, an attempt at compensation on the part of the human being in the manufacture of embryonic or deficient tissue to attempt to assume the function of normal, mature structure.

Dr. Skoog (closing).—I am interested in the inflammatory condition shown sometimes in the brain tissue. Sections around the small vessels at times suggest lesions such as we see in the various types of encephalitis, including epidemic.

LICHEN PLANUS TREATED WITH BISMUTH ARSPHENAMINE SULFONATE (BISMARSEN)*

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In many patients with lichen planus, difficulty is encountered in inducing involution of the lesions. It is well known that the eruption on the buccal mucosa, tongue and lips and also the lesions on the glans penis are usually the last to disappear, if indeed they disappear at all. With this in mind, another drug was sought with the idea of finding a remedy which might have a more profound and lasting effect than the drugs hitherto used.

Mercury, arsenic and bismuth, singly or in combination, have been employed in the treatment of lichen planus both orally and parenterally for many years and when these were used in combination with x-ray many of the cases cleared up. However, relapses were frequent. It was therefore decided to try a combination of arsenic and bismuth, namely, bismarsen.† The pharmacology and toxicology of this drug are well known; therefore it recommended itself to us for trial. Chemically it is bismuth arsphenamine sulfonate, a brownish-yellow amorphous powder, readily soluble in water, with an arsenic content of about 13 per cent and a bismuth content of about 23 per cent. It is administered intramuscularly; but certain precautions, to be described later, must be observed. It is of course important that during the course of this treatment the patient should be watched for all of the phenomena indicating idiosyncrasy to arsenic and bismuth.

We report here a series of cases selected from the skin clinic of the Barnard Free Skin and Cancer Hospital and a few from two private practices. A variety of forms of lichen planus are included, the hypertrophic, the generalized, the localized, one having only oral lesions and one which developed during the treatment of another disease with bismarsen.

Case 1.—Miss C. L., a 30-year-old white woman, was seen on February 14, 1939. She said that the onset of her disease occurred 3 weeks prior to her admission to the clinic. She revealed a typical eruption of lichen planus on the skin and buccal mucous membranes. Twelve intramuscular injections of bismarsen were given at weekly intervals, or a total dosage of 2.0 grams. The course of the disease showed constant improvement and on May 23, 1939, no lesions could be found either on the skin or buccal mucosa. She reappeared in the clinic on September 22, 1939, at which time she was found to have lichen planus on both lips. A series of ten injections of bismarsen was given with considerable improvement when she was last seen on October 24, 1939 (*Figs. 1* and *2*).

Case 2.—Mr. J. C., a 48-year-old white male, was admitted to the clinic on February 27, 1939. The patient stated that the disease had begun some three months prior to admission. He had lichen planus lesions confined to the tongue. A 1-plus Kahn test was obtained on routine serologic examination and he was placed on mixed treatment for a period of two weeks with no benefit to his lesions. A second Kahn test was done and the result was negative. The diagnosis of lichen planus of the buccal mucosa membrane was confirmed by biopsy. Treatment with arsenic trioxide and vitamin B complex resulted in no improvement. On May 10, 1939, he was started on bismarsen therapy and after eight injections some improvement was noted. Scarcity of the drug at that time made it necessary to discontinue the treatment and he was given injections of bismuth potassium tartrate for one month, during which period the lesions showed no improvement. On July 19, 1939, bismarsen treatment was resumed with steady and constant improvement. Sixteen injections were given, or a total of 3.0 grams of bismarsen. When he was examined on August 25, 1939, all of the lesions in his mouth had disappeared. On October 6, 1939, he reappeared in the clinic with lichen planus lesions on the buccal mucous membrane. When he was last ex-

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†We are indebted to the Dermatological Research Laboratories, a division of the Abbott Laboratories, for the bismarsen used in this investigation.

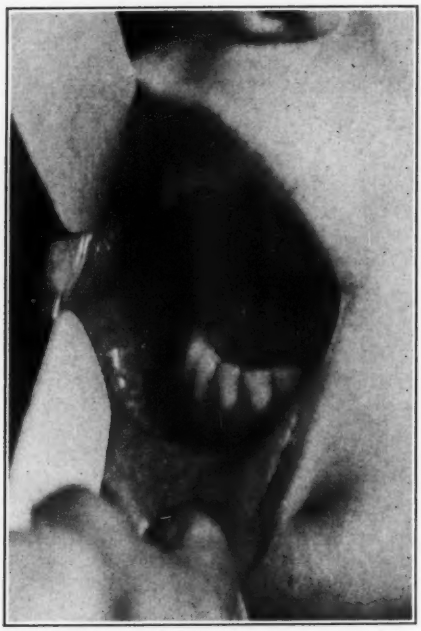

Fig. 1, Case 1
Mucous membrane lesions before treatment.

Fig. 2, Case 1
Mucous membrane after treatment.

amined on October 20, 1939, these lesions seemed to be improving.

Case 3.—Mr. F. G. (No. 74259), a 50-year-old white man, entered the clinic November 19, 1938, with the history that his disease had started approximately one year previously. He presented an eruption of lichen planus, confined to the legs and hands. After three injections of 0.1 grams each of bismarsen, drowsiness and generalized malaise were noted. The drug was discontinued and when he appeared ten days later an erythematous rash was found on his arms which was considered to be arsenical dermatitis and the treatment was stopped.

Case 4.—Mrs. M. S. (No. 73614), a 55-year-old white woman, entered the clinic on August 30, 1938, with what was apparently a contact dermatitis. She gave a history that the eruption had begun one month previously. The eruption was present on the hands, forearms, neck and slightly on the face. When she was again seen on September 30, 1938, typical lesions of lichen planus were found on the forearms and trunk and the patient was placed on treatment of mercury with chalk by mouth, with little or no improvement. On October 1, 1938 bismarsen therapy was started and a series of ten injections was given, or a total dosage of 1.1 grams of the drug. On February 1, 1939, there was no evidence of active lichen planus, only pigmentation remaining. She reappeared in the clinic on March 8, 1939, with a relapse. Bismarsen therapy was resumed with very little improvement. It was discontinued on May 9, 1939, and the patient was placed on arsenic trioxide by mouth with no improvement. On June 14, 1939, bismarsen therapy was started again, but when she had received a total of 0.7 grams, stomatitis developed and treatment had to be discontinued for two weeks. The patient was again placed on bismarsen therapy, a total of 0.6 grams, and when seen on October 10, 1939, the lichen planus had completely involuted.

Case 5.—Mr. R. B. (No. 73110), a 36 year-old white man, was admitted to the clinic on July 20, 1938. He stated that the disease had begun about three months previous to his entering. He presented typical lichen planus lesions confined to the scrotum. Intensive treatment with mercury bichloride intramuscularly and protiodide of mercury by mouth resulted in no improvement. On November 28, 1938, bismuth potassium tartrate was started and given at weekly intervals intramuscularly. He was given sixteen such injections, but new lesions were constantly appearing, so on April 21, 1939, he was given his first injection of bismarsen. He did not report to the clinic again until July 17, 1939, when he was again placed on bismarsen. After fourteen injections, or a total of 2.8 grams, definite improvement was obtained and when he was last seen on October 21, 1939, marked improvement was noticed. During the course of the bismarsen therapy some signs of arsenical dermatitis were noted, but the patient was given large doses of vitamin C and these disappeared.

Case 6.—Mrs. T. H. (No. 77375), a 54-year old white woman, entered the clinic on July 25, 1939. The onset of the disease was approximately three months prior to entering. She displayed typical lichen planus lesions on the buccal mucous membrane and on the legs and wrists. After ten injections of bismarsen, a total dosage

of 1.5 grams, the patient began to show signs of arsenical intoxication. In this case the injections were continued, but the patient was given 200 milligrams of vitamin C per day, which seemed to control the eczematous phenomena. The patient seemed to respond very well to the vitamin C treatment and the treatment was continued in smaller maintenance doses of 100 milligrams daily. A total of twenty injections of bismarsen (2.7 grams of the drug) was given, resulting in the total disappearance of all of the lesions by October 20, 1939.

Case 7.—Mr. G. W. (No. 77353), a 41-year-old white man, entered the clinic on July 24, 1939. He gave a history that the onset of the disease had occurred some twenty years previous to his admission. He showed a very extensive hypertrophic type of lichen planus on the legs and a moderate papular type on the wrists. After ten injections of bismarsen the lesions on the legs had decreased in size and extent. By October 24, 1939, he had received twenty-five injections, or a total dosage of 3.3 grams. At that time the lesions of the wrists had cleared and the hypertrophic lesions on the legs were undergoing definite regression. X-ray was not used on the hypertrophic lesions because it was decided to see what effect the bismarsen would have on this type of lichen planus.

Case 8.—Mr. V. Z. (No. 74130), a 50-year-old white man, was admitted to the clinic on November 11, 1938. The onset of the disease had been two months before admission. He presented a generalized eruption of lichen planus with lesions also on the glans penis and buccal mucosa. A series of twelve injections, or a total of 1.5 grams of bismarsen, were given, resulting in the disappearance of all of the lesions by January 19, 1939, except for one papule on the glans penis. No further injections of bismarsen were given and when observed on August 7, 1939, the penile lesion was still present. He was then placed on arsenic trioxide and when observed on September 12, 1939, the lesion on the glans penis still persisted.

Case 9.—Mrs. I. R. (No. 76258), a 25-year-old white woman, was first seen in the clinic on April 4, 1939. She gave a history that the disease had begun some three months previously. She presented typical lichen planus lesions below the right knee and on the lateral surface of the left ankle joint. Treatment with arsenic trioxide internally was of no avail and on July 21, 1939, bismarsen injections were started. There was a slow but steadily progressive improvement with loss of subjective symptoms and involution of the lesions. She received twenty-two injections of the drug, or a total dosage of 3.1 grams, and by October 17, 1939, she was entirely clear, only pigmentation remaining at the sites of the former lesions.

Case 10.—Mrs. A. S. (No. 77078), a 65-year-old white woman, entered the clinic on July 3, 1939. She gave a history that the disease had begun some three months previously. The eruption was fairly generalized, but thickest on the limbs. She also had lesions on the buccal mucosa. Twenty injections of bismarsen were given, a total of 3.2 grams. She showed a few new lesions up to the time of her third injection. After that no new lesions appeared. The pruritus disappeared and by October 6, 1939, the disease had completely involuted, including the lesions on the buccal mucous membranes.

Case 11.—Mrs. L. McG. (No. 77111), a 54-year-old white woman, entered the clinic on July 5, 1939, with a generalized eruption of lichen planus which had been present for three months. She was immediately placed on bismarsen therapy and received a total of 2.6 grams in a series of twenty injections. The pruritus disappeared and the lesions began to involute after the seventh injection. When examined on October 3, 1939, she was entirely free of lesions (*Figs. 3, 4, 5* and *6*).

Case 12.—Mrs. E. W. (No. 76085), a 48-year-old white woman, entered the clinic on April 12, 1939. She presented an eruption of lichen planus involving the arms, legs, thighs and buttocks. The lesions on the legs were somewhat hypertrophic. On mercury by mouth and later on arsenic trioxide by mouth she made some slight improvement, but it was very slow and unsatisfactory. On July 24, 1939, she was placed on bismarsen therapy, receiving a total of twenty injections, or a total dosage of 2.6 grams. After these injections were started her favorable progress was constant and by October 13, 1939, when she was last observed, there was only pigmentation left (*Figs. 7, 8, 9* and *10*).

Case 13.—Mr. S. G. (No. 76688), a 61-year-old white man, entered the clinic June 31, 1939, complaining of an itching eruption on the forearms and legs which he stated had appeared about three weeks before admission. He presented typical lichen planus and was given arsenic trioxide by mouth. Only slight improvement was obtained and on July 17, 1939, injections of bismarsen were started. By October 20, 1939, he had received fourteen injections, or a total dosage of 2.2 grams. At that time there were still a few lesions on the posterior aspects of both legs, all of the other lesions having disappeared.

Case 14.—Mr. F. G. (No. 18378), a 38-year-old white man, was treated in the clinic in 1918 for lichen planus by intramuscular injections of bichloride of mercury. He was discharged apparently free of lesions after three months of treatment, but returned on July 18, 1939, 21 years later, with a recurrence. At that time questioning revealed that there had been persistence of papules in the palms ever since the first attack, although he had received a course of bichloride of mercury injections from a private physician in 1928. Bismarsen therapy was started and after four injections the subjective symptoms had disappeared and the lesions had improved. Up to October 24, 1939, he had received a total of twenty-four injections of bismarsen, or a total dosage of 3.7 grams, at which time it was noted that he had made considerable improvement.

Case 15.—Mr. J. G. (No. 78034), a 66-year-old white man, entered the clinic on September 18, 1939, with a history that his skin eruption had begun some six weeks previously. He presented typical lichen planus distributed on the trunk and arms and he also had oral lesions. After six injections the lesions began to fade rapidly and on October 24, 1939, after having received eleven injections, or a total dosage of 1.1 grams, he was entirely clear except for some lesions on an area over the suprasternal notch and a few remaining lesions on the buccal mucous membrane.

Case 16.—Mr. E. S. (No. 77775), a 45-year old white man, entered the clinic on August 25, 1939, with a history that an eruption began on his legs eleven years previously and that it had spread considerably in the

Fig. 3, Case 11
Lesions on forearms and hands before treatment.

Fig. 5, Case 11
Lesions on thighs and legs before treatment.

Fig. 4, Case 11
Forearms after treatment.

Fig. 6, Case 11
Thighs after treatment.

Fig. 7, Case 12
Lesions on thighs before treatment.

Fig. 9, Case 12
Lesions on forearms before treatment.

Fig. 8, Case 12
Thighs after treatment.

Fig. 10, Case 12
Forearms after treatment.

preceding three months. He presented a typical eruption of lichen planus on the legs and in the mouth with beginning lesions on the wrists. Bismarsen therapy was started on September 1, 1939, and improvement was noted after the first few injections. By October 24, 1939, he had received sixteen injections, or a total dosage of 1.6 grams of the drug, and the lesions had almost completely involuted.

Case 17.—Mrs. L. K. (No. 73671), a 33-year-old white woman, was admitted to the clinic on September 2, 1938, with an eruption which she said had begun two months previously. She was treated with mercury, bismuth and arsenic trioxide and by June, 1939, she was apparently cured and was discharged. On September 15, 1939, she returned to the clinic with a relapse of the eruption on the right wrist and right foot. She was placed on bismarsen therapy and by October 24, 1939, she had received twelve injections, or a total of 1.2 grams, and the lesions had very markedly improved.

Case 18.—Mrs. B. L. (No. 37647), a 46-year-old white woman, appeared in the clinic on September 22, 1939, with typical lesions of lichen planus involving almost the entire skin. She stated that this had been present for about two weeks. She was placed on bismarsen therapy immediately and by October 13, 1939, she had received six injections of 0.1 grams and was showing definite improvement. On that day she reported with a thrombophlebitis involving the left thigh. Bismarsen treatment was discontinued. One week later marked maceration of the eruption developed beneath the breasts. On her appearance the following week more lesions of lichen planus began to appear. She was sent into the hospital, bismarsen therapy was continued and she is at present markedly improved.

Case 19.—Miss H. W. (No. 75568), a 10-year-old white girl, appeared in the clinic on February 2, 1939, with a generalized lichen planus. She was given mercury with chalk by mouth and when seen on April 24, 1939, was greatly improved. She did not reappear in the clinic until September 12, 1939, at which time she had a total recurrence of the eruption, lesions being present even on the soles of the feet. She was started on bismarsen therapy immediately, the beginning dose being 0.05 grams and then raised to 0.1 grams. This was tolerated very well and it was continued at biweekly intervals. Her progress was slow until her thirteenth injection, at which time it was noted that the lesions had greatly improved. Up to October 23, 1939, she had received thirteen injections, or a total of 1.25 grams of the drug.

Case 20.—Mr. B. A. (No. 77216), a 36-year-old white man, entered the clinic on July 14, 1939, with typical psoriasis. At that time we were treating a few cases of this disease with bismarsen and he was placed on injections of this drug. After having received eleven injections of bismarsen for a total of 1.6 grams he developed a typical lichen planus of the forearms (*Figs. 11* and *12*). We interpreted this as activation of latent lichen planus by arsenical treatment. Treatment, however, was continued with bismarsen and after four more injections the lichen planus began to involute and by the time he had received his twenty-first injection, or a total of 3.0 grams of the drug, these lesions had disappeared. No effect was observed upon the psoriasis lesions.

Case 21.—Mrs. L. B., a 54-year-old white woman, private patient of Drs. Engman and Engman, was first seen on July 17, 1939. At that time she presented a very

Fig. 11, Case 20
Lesions on forearms before treatment.

Fig. 12, Case 20
Forearms after treatment.

severe generalized lichen planus with a few hypertrophic lesions. She was placed on bismarsen therapy and after eleven injections of 0.1 grams of the drug all of the lesions had completely involuted.

Case 22.—Mrs. A. C., a 71-year-old white woman, private patient of Drs. Engman and Engman, was first seen on July 29, 1939, at which time she presented a generalized lichen planus which had been present for several months. Living at a considerable distance from St. Louis, she was referred back to her own physician and he was advised to give her 0.1 grams of bismarsen every four or five days. When seen on September 15, 1939, she was greatly improved. When last seen on October 31, 1939, the eruption had entirely cleared up following sixteen injections of 0.1 grams, or a total dosage of 1.6 grams of the drug.

Case 23.—Mrs. E. R., a 58-year old white woman, private patient of Drs. Engman and Engman, was first seen on September 13, 1939, at which time she presented a generalized lichen planus with a superimposed chemical dermatitis. The lichen planus had appeared some months previously. She was placed on bismarsen therapy and was last seen on October 17, 1939, by which time she had received seven injections, or a total of 1.05 grams of the drug. On October 5, 1939, it was noted that she had shown a moderate amount of improvement, but a few new lesions had appeared. On her last visit on October 30, 1939, it was noted that she was very much improved.

Case 24.—Mrs. G. W., a 50-year-old white woman, private patient of Dr. Conrad, Sr., was seen on October 28, 1938, with a generalized eruption of lichen planus which she said had been present for two or three years. She was treated with mercury, arsenic trioxide and x-ray with little or no results. On September 18, 1939, she was placed on bismarsen therapy. After her third injection the pruritus began to subside and after her seventh injection the lesions were beginning to involute. On September 11, 1939, she showed a faint papular eczematous eruption which was interpreted as an early sign of arsenical dermatitis. She was given large doses of vitamin C and the injections of bismarsen were continued until she had received twelve injections, or a total of 1.5 grams of the drug. After the twelfth injection the eruption had completely disappeared and the dermatitis had also cleared up.

Case 25.—Mr. F. B., a 34-year-old white man, private patient of Dr. Conrad, Sr., was first seen on July 28, 1939, with a generalized eruption of lichen planus. He was treated with arsenic trioxide with little effect and on August 30, 1939, bismarsen treatment was started. After five injections, or a total of 0 55 grams of the drug, he developed signs of drowsiness, stomatitis and puffiness about the eyes. He was given large doses of vitamin C and the injections were continued. The toxic symptoms disappeared promptly and after seven injections of bismarsen all of the lichen planus had disappeared and to date he has been free from recurrence.

DISCUSSION

The use of bismuth arsphenamine sulfonate in the treatment of syphilis is of course well known. We followed out one of the recommended plans for the administration of the drug in the treatment of lichen planus. This plan consisted of four intramuscular injections of 0.1 grams at biweekly intervals and then the dose was raised to 0.2 grams. We continued this plan for some time and during a period when we were temporarily short of the drug we began to give the patients 0.1 grams. This was continued for about two weeks. When a new supply of the drug was received it was found that during this period the dose of 0.1 grams seemed to produce as much change in the lesions as did the dose of 0.2 grams; therefore, experimentation was begun with variations in the dosage. Some patients were placed on 0.1 grams from the start, others were allowed to follow the first method mentioned and some were allowed to continue on doses of 0.1 grams after having been dropped from 0.2 grams. Some patients were given two injections a week and some, one injection a week. It was found that improvement was much more rapid when injections were given twice weekly. We therefore concluded that the best plan of treatment consisted in giving injections of 0.1 grams of this drug twice weekly.

Of course the usual minor reactions to bismarsen treatment were encountered. In most patients the first few injections caused some discomfort, but with the continuance of treatment this was less frequent. Local reactions consisted chiefly of erythema, induration and moderate pain at the site of the injection, with some inhibition of hip joint movements. We found that these could be avoided or lessened by using a longer needle with a smaller diameter (a 3-inch needle of 21 gauge). It is necessary to avoid inserting the needle into a vein, and moreover to make certain that none of the solution is deposited in the needle track. Our technic, therefore, is to mix the drug in the ampoule by employing a larger gauge needle, filling the syringe, discarding that needle and then using another needle of the proper gauge and length for the injection. This needle is attached to the syringe, is inserted in the upper outer quadrant of the buttock and the syringe disconnected. We then wait for one full minute to see if blood will flow through the lumen of the needle. If it does not,* the syringe is connected and the injection made slowly.

Dr. Roy Kile informs us of an unusually severe type of reaction that he encountered in a patient. A woman,

*It is not enough to pull back on the plunger to see whether blood can be aspirated. The bevel of the needle may be against the wall of the vein and the negative pressure exerted by the syringe may be sufficient to pull the wall of the vein against the bevel of the needle. This would prevent blood from appearing in the syringe, although the needle may be in the vein.

after receiving a small dose of bismarsen, immediately noticed a generalized itching and, after receiving a larger dose the second time, had an urticarial reaction with chill, nausea and weakness. After two doses of 0.5 c. c. of epinephrine, the reaction subsided. The temperature was subnormal and the pulse full. It was not a shock type of reaction. Dr. Kile says that he was sure that the drug was not introduced into the vein.

We have noted three cases of stomatitis, several cases of puffiness of the eyelids, and two or three cases of apparent arsenical reaction on the skin. Some of them we were able to control by administration of large doses of vitamin C; others we felt had to be taken off of the treatment for fear of severe complications. All of our patients had a complete medical examination, including blood counts and urinalysis, before starting the use of the drug and leukocyte counts and urinalyses were done from time to time on every case. We were thus able to eliminate from our series those cases in which we felt bismarsen might be contraindicated. The contraindications to the use of this drug include cachexia, severe anemia, endocrine disturbances, advanced tuberculosis of the lungs, cardiac insufficiency, hemorrhages, epilepsy and alcoholism. All of our cases which showed marked renal disturbances were also eliminated or the drug was given with extreme caution and with frequent urinalyses.

In a discussion of the results one must take into consideration the duration of the disease. The more chronic and longer lasting the disorder, the longer the time necessary to secure involution. This also holds true in the number of injections necessary to relieve the subjective symptoms. We have found that the shorter the duration of the disease, the fewer the number of the injections necessary to relieve the pruritus and the fewer the number of injections needed to effect an apparent cure.

In the usual case of three to four months' duration, the patients experience relief of subjective symptoms following the fifth or sixth injection and an apparent cure may be accomplished by fifteen or twenty injections. In the more chronic cases where the disease has been present for months or years, and especially where the lesions have become hypertrophic, the number of injections to effect relief or apparent cure must be increased. In some cases the hypertrophic lesions began to show evidence of involution after about the tenth injection and from that time on many showed a definite tendency to decrease in size. The pruritus, while still present in these patients of the hypertrophic type, definitely decreased and the patients usually were much more comfortable.

We have found this treatment to offer better prospects in the treatment of lesions of the mucous membranes. In our series of twenty-five cases there were seven cases of involvement of the oral mucous membrane, all of which cleared up, but two relapsed. One case showed involvement of the glans penis, which failed to clear up under this therapy. We encountered only one case of early arsenical dermatitis following three injections of bismarsen. Two or three others showed signs of arsenical dermatitis, but seemed to clear up on the administration of large doses of vitamin C. We feel that it will be advantageous in the future to place all patients who are receiving this treatment on vitamin C therapy as well.

CONCLUSION

Bismuth arsphenamine sulfonate (bismarsen) seems to be of value in the treatment of lichen planus. However, the series of cases reported here is small and more work must be done with the drug before any final conclusion can be reached as to its value. We offer it as another method of attack in the treatment of lichen planus and we suggest that it may be especially useful in those cases with mucous membrane involvement.

DISCUSSION (*Abstract*)

Dr. Thomas W. Murrell, Richmond, Va.—Many of the conclusions that would come from this paper are impressions, but impressions from master clinicians, such as Dr. Conrad and Dr. Weiss, can be practically accepted as factual evidence.

As I understand it the authors are presenting this remedy as a remedy which they feel is superior to those ordinarily used.

Dr. Conrad has mentioned oral administration. I do not think it is fair to compare drugs used intramuscularly with those used orally. Bichloride of mercury is very much superior used intramuscularly. It seems to me that bismarsen possesses hazards that are not associated with the use of bichloride and bismuth, and some of the results shown from bismarsen have been duplicated quite as brilliantly by the older methods. Now if we get hold of cases that the older methods benefit, I do not see the particular necessity of using bismarsen if bismarsen has a higher hazard rate. In other words, if we have to give our patients vitamin C to avoid hazards and run into the other dangers, it is better to use bichloride or bismuth as a routine and to reserve bismarsen for cases that other drugs do not help, that is, for the recalcitrant cases.

In reading Dr. Conrad's paper, I thought of Dr. Roussel's paper read in San Antonio on the use of anthrax vaccine in leprosy. He said that his results were so

good with the anesthetic type of leprosy and so bad with the nodular type that he sometimes wondered whether he was dealing with the same condition. We use gold in the treatment of lupus erythematosus and get such brilliant results with the plaque type and such very poor results with the disseminated type, that many men are concluding that they are not treating the same disease.

This summer we had a case of lichen planus under treatment, a disseminated rash over the legs and forearms and one large verrucous lesion near the right knee. Just before I left home I saw that patient and all of the smaller disseminated rash had gone, leaving the pigmentation that normally follows treatment, with no itching. The verrucous lesion was absolutely untouched. I have talked with several men about this case and it seems to me that if the verrucous lesion is of exactly the same etiology as the disseminated lesion, we ought to get some parallel results in the treatment. Apparently we do not. Consequently we are going to switch over to x-ray on the hypertrophic lesion.

Dr. Emmett R. Hall, Memphis, Tenn.—I have had a number of cases of chronic lichen planus in the last year or two that have caused me considerable worry. I should like to ask Dr. Conrad whether he has used "enesol," a combination of arsenic and mercury, and how he thinks "enesol" compares with bismarsen.

Dr. Harry M. Robinson, Baltimore, Md.—I wish to discuss the case of psoriasis which Dr. Conrad reported which, while being treated with bismarsen, developed lichen planus. We have had quite a few patients with syphilis who, on being treated with the various arsenicals, developed a lichen planus-like eruption. I believe that McCafferty was the first in this country to discuss that type of post-arsphenamine eruption several years ago. At least 0.5 per cent of our eruptions are of the lichen planus-like type. However, contrary to Dr. Conrad's experience, the eruption in our cases persists. Clinically the lesions resemble lichen planus.

Lastly, a word of caution concerning the use of bismarsen. For several years I have used this drug in the treatment of syphilis and discarded it as a routine for two reasons: first, it was not especially efficacious in the treatment of syphilis, and secondly, it caused serious reactions. In lichen planus we deal with a condition that itches and with bismarsen we deal with a drug which occasionally causes itching. I would only add a word of caution to those who administer bismarsen. Noting Dr. Conrad's results, I intend using it in a few cases; increase in itching or eruption shall be a signal to discontinue the drug.

Dr. Conrad (closing).—This drug does have some hazards. We too have given both bismuth and mercury intramuscularly and have obtained good results. We have offered this only as another method of attack. I do not think there is anything new in it because it is very similar, to answer Dr. Hall, to that supposed combination of bismuth and mercury, "enesol." We wrote to Dr. Andrews in New York about "enesol" when we started on this work and he was unable to tell us its formula. The American Medical Association reported that "enesol" was not an accepted drug since their chemists were unable to verify the supposed formula. Dr. Andrews also informed us that he was of the opinion that neither arsenic nor mercury was found in this compound. Perhaps this was due to the fact that the manufacturer failed to give a formula by which the composition of the substance could be determined.

In the patient with psoriasis who was being treated with bismarsen, in an experimental way, and who developed lichen planus lesions that cleared up with the continued use of the drug, the lesions were biopsied and microscopic studies proved the diagnosis of lichen planus.

A CASE OF MARKED EOSINOPHILIA*

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R. B., a white waitress, aged 22, upon applying for a health card was found to be syphilitic in June, 1937. Her only complaints were loss of appetite and a feeling that she was not wholly as well as usual. Intensive antisyphilitic treatment was begun at once, with 8 injections of bismuth salicylate, given twice weekly, followed by intravenous neoarsphenamine in ordinary dosages, also semiweekly. Of the latter drug she received 9 injections. There was nausea following the first three, but the patient was not incapacitated. After the seventh she noticed dull pain in the right lower chest, which was not intensified by deep breathing. At about the same time the skin and sclerae became icteric, and the lower chest pain seemed to move to the right upper abdominal quadrant. This was accompanied by slight fever and there was discomfort when she lay on her right side. The jaundice was treated with a tablet taken at bedtime and epsom salts in the morning. Within a week the pain had left and the patient stated that her skin cleared up, although the sclerae were still yellow. On the day she was to have had the seventh of nine injections of neoarsphenamine which she received, she was awakened by itching of the skin and appearance of small red spots all over the body. There was also swelling of the hands and eyelids. In twenty-four hours the skin took on a generalized redness. The second day there was fever. The red rash continued and was present when she was admitted to the hospital on August 3, 1937, at which time there was, in addition to the above symptoms, swelling of the lower extremities. Hematuria was also present. The early past history was not important except for frequent chest colds. There was, however, definite evidence of an allergic background in that tomatoes were avoided because they produced hives. She also stated that as a child both she and other members of her family had had eczematoid rashes on their forearms that cleared up with treatment. Her catamenia was normal. Four years previously she had had malaria, which was cured by quinine therapy. At the age of 8 she had ground itch and was treated for hookworm when she was 10, but there were no subsequent stool examinations. The family history offered nothing of importance, except

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Fig. 1
Skin showing marked exfoliation.

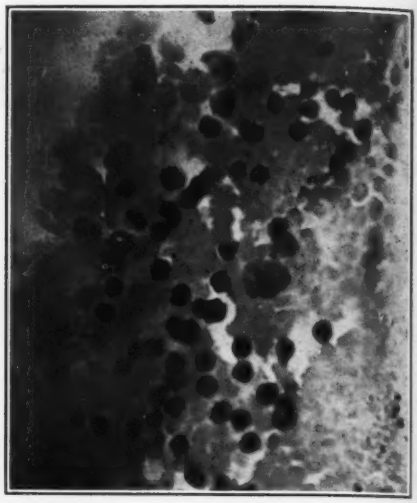

Fig. 2
Blood film showing eosinophilia almost to exclusion of other leukocytes.

that the mother, who died of mammary cancer, had migraine. Except for this there was no other familial history of allergy.

The patient was married at 16, but the marriage was annulled immediately. She had recently lost sixteen pounds, her average weight being 131 pounds.

Examination of the patient revealed the above findings, the most prominent of which was the bright red coloration of the skin. She was a red-haired blond, with the usual light skin. The systems were normal.

A diagnosis of arsenical dermatitis was confirmed by Dr. J. Frank Wilson, of the dermatologic service, and treatment consisted of intravenous injections of sodium thiosulphate, followed by 2 per cent sulphur ointment in cold creams for the exfoliation. Progress in the hospital was satisfactory. Her temperature rose to 103° F. and remained there, with slight remissions, for five days, gradually receding to normal during the following five weeks. Exfoliation began rather extensively on August 6. The only other symptom that persisted was the upper abdominal pain. The hematuria proved to be transient. Desquamation continued until August 22, the nineteenth day after admission, at which time a mild eruption developed and was followed by even more severe exfoliation and generalized itching. At the end of six weeks the body still showed roughening.

A persistent hookworm infection was discovered during the hospital stay, for which treatment was also given.

The final diagnosis was as follows: syphilis, exfoliative dermatitis following neoarsphenamine medication, uncinariasis, arsenical nephritis, and marked eosinophilia.

REMARKS AND LABORATORY FINDINGS

The blood serum Kahn reaction was negative during

BLOOD STUDIES

	8/6/37	8/18/37	8/20/37	8/24/37	8/27/37	8/30/37
RBC	3,070,000	3,330,000				
WBC	4,700	30,000	45,450	40,450	40,750	50,800
Hemoglobin (Sahli) per cent	62					
Eosinophils, per cent				75	83	90
	9/6/37	9/7/37	9/10/37	9/14/37	9/21/37	
RBC		3,560,000		3,900,000		
WBC	18,800	13,500	13,950	10,850	10,650	
Eosinophils, per cent	61	55	49	29	35	
	10/7/37	10/11/37				
RBC						
WBC	10,800	9,900				
Eosinophils, per cent	28	29				

hospitalization. The urine contained traces of glucose and numerous erythrocytes on admission, accompanied by a four-plus albumin content (sulfosalicylic acid method). This all cleared up after the third day.

Examination of the feces shortly after admission brought to light the presence of hookworms and ova.

The blood urea clearance upon admission was 15.3 per cent of normal for the first hour, and 25.3 per cent of normal for the second hour. Metabolic blood chemical examinations were practically normal, following a slight increase in nitrogen retention and a cholesterol of 250 mg. per cent. The basal metabolic rate was minus 8 after recovery.

Routine blood studies showed a steadily increasing leukocyte count, accompanied by a marked increase in the eosinophils to 90 per cent, which condition prompted the citation of this case.

This remarkable eosinophilia may have been influenced by the intensity of the dermatitis because of the allergic tendency, augmented by the presence of an active hookworm infection. Other sources of extreme eosinophilia such as trichinosis were ruled out. The eosinophils were apparently fully mature in all cases. In the matter of staining technic, blood films were fixed in Merck's reagent grade methyl alcohol and stained by Giemsa's method. Photomicrographs show the great preponderance of these cells over all others. A lantern slide in color photomicrography brings them out beautifully.

KIDNEY SALVAGE*

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In presenting the subject of the recuperative power of the kidneys we do not wish to imply that regeneration actually takes place in the kidneys, but that, depending upon certain factors, these organs have a remarkable ability to repair. This repair is so striking in the cases that we have selected to show you that it makes little difference whether it is regeneration, hypertrophy, or what not; clinically the result is the same. They were infected, showed no response to the ordinary functional test, and pyelographic study showed severe grades of kidney destruction, and yet, by simple drainage and removal of the obstruction, they returned to normal with a function as good or better than that of the opposite side. However, we realize that there are kidney conditions in which to be conservative is not to be conservative. There must be some kidney structure present, for it is not conceivable that a kidney with no function and no parenchyma, as in pyonephrosis, should ever return to normal. Conservative surgery in such cases would not be justified.

Rupture of the kidney is an example of acute damage which is usually not an indication for radical surgery, as we were at one time led to believe. If one will recall that the arteries of the kidney are end arteries, that they do not anastomose, and that a rupture takes place, as a rule, between these arteries, it is not difficult to understand that severe grades of rupture will heal and leave only a small amount of scar. The venous bleeding can usually be controlled by drainage when it is severe.

Grayson Carroll[1] reported a case of badly damaged ptosed kidney that recovered completely on suspension, although the patient was advised to have a nephrectomy. A few years ago Walters[2] presented a series of cases in which he carried out plastic operations on the kidney pelves and ureters. They were markedly dilated, with damage to the kidneys. His operative results were excellent. Kretschmer[3] has called attention to the interesting fact that the ureters and renal pelves consistently dilate during pregnancy. Lee and Mengert, in a series of pre- and postpartum intravenous urograms, showed the completeness and promptness with which these dilated upper urinary tracts of pregnancy returned to normal after delivery. In a personal communication Wesson,[4] of San Francisco, said that in Germany they do not appreciate the value of conserving kidney structure. They frequently remove a kidney because of stone, even though it is not badly damaged, and much to their chagrin they are now seeing more cases of stone in single kidneys.

In spite of the improvements in the methods of diagnosis, the various tests are not always accurate. Cabot[5] has repeatedly called attention to the fallacy of tests for renal function in the presence of stone or an obstructive lesion. No dye or intravenous skiodan may appear from the involved kidney, and yet it may not be a dead one. A study of the blood chemical constituents may not help, for the function of both kidneys must be impaired, as a rule, to cause retention of nitrogen in the blood. Also, serious

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renal damage may be present without commensurate findings in the urine. For instance, a blockage of the ureter on the affected side can cause error in the interpretation of the bladder urine. Another source of error from the examination of the urine is in cortical abscesses of the kidney. In such cases the urine may show little, if any, change. According to Joly,[6] still another source of error is a cessation in growth of a stone that has been observed over a period of years. This cessation may be a bad, instead of a good, sign. The stone may be lodged in a functionless kidney. Pain, a common symptom, cannot be relied upon to indicate the amount of damage sustained by the kidney. It is usually a good sign, however, that the kidney has some excretory value, for a functionless organ is usually painless. Because of these discrepancies there are times when the true condition of the kidney can be determined only at operation.

When the problem of a damaged kidney, with no function but with some parenchyma, presents itself at operation, one must of course try to determine the amount of kidney structure present and the ability of the kidney to function properly after it is drained. We realize that some of these cases will go on to complete destruction, but others will recover. The reasons in each case are not well established.

Hinman[7] says that the question of renal counterbalance has to be considered in these cases. According to his theory,

> "The kidney, after sustaining a temporary injury, as for example, a temporary period of ureteral obstruction causing hydronephrosis, will go on to complete, or almost complete atrophy if allowed to function in competition with its hypertrophic mate. Thus, if the ureter of the kidney is obstructed for two or three weeks, this kidney becomes hydronephrotic and its mate undergoes hypertrophy. If, at the end of this time, the obstruction to the ureter is relieved, the hydronephrotic kidney supposedly will be placed at a distinct disadvantage. According to the theory of renal counterbalance, the kidneys enter into functional competition, and the weaker kidney eventually goes on to complete, or almost complete, atrophy."

Hinman assumes that hypertrophy of the opposite kidney takes place in all cases, with atrophy of the bad one. Should this be strictly true, there would be no need to be conservative in these cases, and we have proof that there are patients living today on the bad kidney as to the removal of which there was a debate in the past. In his experimental work Hinman was dealing more or less with aseptic processes, and the atrophy he referred to was one of disuse, and not due to infection, whereas clinically we have to contend with infection as well. There are also degenerative changes to be considered in the opposite kidney, as well as hypertrophy. The outcome, to some extent, depends on which takes place.

Joelson,[8] in his experimental work, did not demonstrate this renal atrophy of disuse, as did Hinman, and he says that the theory of renal counterbalance need not be seriously considered in deciding on surgical treatment of certain renal lesions. Cabot and Quinby also say that it lacks confirmation. However, Hinman's and Joelson's experiments coincided when it came to the injured kidney's undergoing repair if the demand were placed upon it: that is, when the hypertrophied kidney on the opposite side was removed, the load was then placed on the injured kidney. The injured kidney would then undergo a remarkable degree of repair, showing what it could do if the demand were placed upon it; and in conformity with these experimental results, it seems to be true from our experience that surgical repair of the bad kidney gives best results when the opposite one shows either degenerative changes, or at least has not undergone hypertrophy.

We believe that the ability of the lame structure to come back, or of the remaining part of the damaged kidney to hypertrophy, depends not only upon adequate drainage and the amount of damage done, but, to a great extent, upon the condition of the opposite kidney and the type of infection present. If the opposite kidney has actually undergone complete hypertrophy, that is, has increased in size, has an increased appearance of the dye, with an increase in the output, a badly damaged kidney is not likely to respond to conservative methods.

The other factor to be considered in influencing the recuperative power of the kidneys is the micro-organism causing the infection. The nature of the infection plays an important part in the prognosis. If an organism of the *B. coli* type is found, the kidney is much more liable to recuperate its lost function following a conservative operation than if it is a staphylococcal infection, or other urea-splitting organism. *B. coli* often disappears soon after the removal of the obstruction, or after drainage, but the staphylococcus is much more likely to persist. It is very important, too, to know whether the urine is alkaline or acid. An alkaline urine, as a rule, is more dangerous. So, if pyogenic cocci are found in the urine, the risk in doing a conserva-

tive operation is much greater than if the infection is entirely due to a bacillus of the colon group, and recuperation is less likely to occur.

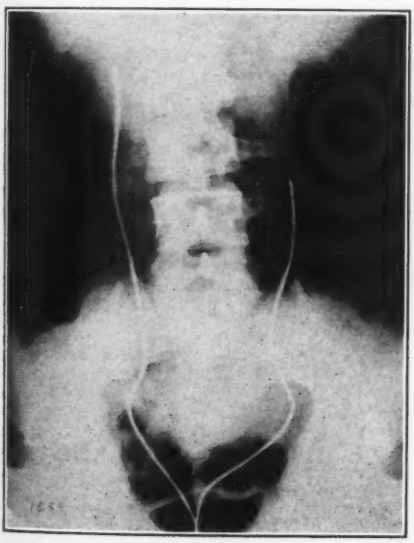
We wish to report the following cases which illustrate the ability of the kidneys to improve when certain factors are present:

Case 1.—J. N. R., a male, aged 53, had had attacks of pain in the left side in the region of the left kidney for seven months prior to the time we saw him. This pain was very severe at times, with elevation in temperature. He was nauseated a good deal. He had some frequency of urination and noticed that his urine was cloudy. Three weeks before he was seen by us a roentgenogram was taken, which showed three shadows in the left kidney region and a small shadow in the region of the prostate. He had been confined in bed for two weeks when we saw him. His past history revealed the fact that he had had an attack of renal colic six years before, at which time he passed blood in his urine and was sick in bed for about three weeks.

Urological Examination.—A catheterized specimen of urine from the bladder showed a moderate number of pus cells, a few red blood cells and many gram-negative bacilli. Stain for tubercle bacilli was negative. Cystoscopic examination revealed a Grade 1 prostatic enlargement. Catheters were passed up both ureters and specimens of urine collected. The right kidney specimen was clear and microscopically showed a few epithelial cells and an occasional leukocyte. The left kidney specimen showed innumerable pus cells and colon-like bacilli. Intravenous dye appeared in four and one-half minutes on the right side, with a 12 per cent output in fifteen minutes, but no dye appeared through the left catheter over the same period of time. A plain roentgenogram was taken with the catheters up each ureter, followed by bilateral pyelograms. In the plain picture the stones can be seen. The bilateral pyelograms showed a ptosed right kidney, but otherwise it was normal. There was no hypertrophy. On

Case 1, Fig. 2

Bilateral pyelogram showing ptosis of the right kidney. The left has marked destructive changes, that is, redundancy of the ureter, dilatation of the pelvis and calices.



Case 1, Fig. 1

Showing three calcified shadows in the left kidney region.

Case 1, Fig. 3

Pyelogram three months after operation. The kidney has practically returned to normal.

the left side there was a redundancy of the ureter, with dilatation of the ureter, renal pelvis, calices, and evidence of marked destruction of the kidney.

Blood chemical examination showed sugar 111, nonprotein nitrogen 40, creatinin 1.5, urea 20 mgs. per 100 c. c. of blood. He was given a blood transfusion and operated upon October 30, 1936. Examination at operation revealed a large, soft, friable kidney, which upon opening drained a quantity of foul urine, with much debris. The kidney itself was hollowed out, with dilatation of all the calyces, but there still remained some cortical structure, although it was felt to be rather thin in places. The stones were removed and a nephrostomy tube inserted. This tube was irrigated at regular intervals until drainage returned clear. It was removed in three weeks and the wound allowed to close.

He returned in three months. A catheterized specimen from the bladder showed eight to ten pus cells per high power field. A stained specimen showed no organisms. Intravenous dye appeared in three and one-half minutes and the output was 12 per cent in fifteen minutes. Skiodan injection shows a remarkable recuperative power of the kidney. In May, 1938, his prostate gland was resected and the stone removed. The patient is now apparently doing well.

Case 2.—Mrs. T. R. P., a woman, aged 44, had had recurring attacks of pain in the left side for twenty years. A catheterized specimen of urine showed many pus cells and colon-like bacilli. A plain roentgenogram showed quite a large stone in the left lower ureter. She was cystoscoped and with some difficulty a catheter was passed up the left ureter. A catheter was easily passed up the right ureter and specimens were collected from each side. The left showed innumerable pus cells and many colon-like bacilli. The right appeared normal. Intravenous dye appeared in four minutes from the right side and in nine minutes from the left side. The output from the right side was 11 per cent in fifteen minutes, and the left showed only a faint trace. Pyeloureterograms done on the left side show a large hydro-

Case 2, Fig. 2
Left pyelo-ureterogram showing large hydronephrotic kidney with clubbing of the calices and tortuous hydro-ureter.

Case 2, Fig. 1
Large left ureteral calculus.

Case 2, Fig. 3
Pyelogram six months after operation. The kidney and ureter are approaching normal.

nephrotic kidney with clubbing of the calyces and a tortuous, large ureter.

The stone in the lower left ureter was removed and two weeks later the left ureteral orifice was fulgurated and then dilated with a large catheter, making the opening considerably larger than normal. Her recovery was uneventful. Six months later, a specimen of urine was essentially negative. Pyelograms showed the kidney and ureter approaching normal. Phenolsulphonephthalein intravenously at this time appeared in five minutes, with a 10 per cent output of the dye in a fifteen-minute specimen.

Case 3.—R. F. B., a man, aged 49, was examined. His roentgenogram brings out two points. Six months prior to the time we saw him he was operated upon and a tube inserted in his left kidney. He told us that at that time a repair operation was done on the pelvis of the left kidney and it was thought that its function would return to normal. Assuming that he was correct when he said that a repair operation was done on the kidney, it brings up this question: had the right kidney been hypertrophied at that time as it is now, as can be seen in the picture, and was the function increased, as it was found by us to be? He had also a unilateral hydronephrosis. Then, if Hinman's theory of renal counterbalance is correct, it would have been useless to operate upon the left kidney and to do any kind of repair operation in the hope that the kidney would return, for the other kidney had already undergone hypertrophy and was practically capable of taking care of all the work, and would have eventually, the left undergoing atrophy. In other words, all the requisites for Hinman's theory of renal counterbalance were present here, plus an infection. The organism from the catheterized specimen from the left kidney showed many gram positive cocci.

Case 3, Fig. 1
Hydronephrotic sac on the left and hypertrophied kidney on the right.

Case 4.—G. T. P., a man, aged 60, history similar to that of the first case: pain in the left side in the region of the left kidney, elevation in temperature, and he was acutely ill. He had been treated for an

Case 4, Fig. 1
Left pyelogram showing marked destructive changes in the kidney.

Case 4, Fig. 2
Pyelogram three months following operation. Kidney has returned to normal.

obscure infection ten months previously and had been in bed practically the entire time.

A bladder specimen of urine showed much pus and many colon bacilli. Catheters were passed up both ureters, the left meeting an obstruction at the ureteropelvic junction by which it would not pass. This drained, however. Specimens of urine were collected. The right specimen showed an occasional pus cell; the left showed quite a number of pus cells, along with colon-like bacilli. Intravenous dye appeared from the right catheter in four minutes. No dye appeared from the left catheter over a period of thirty minutes. The output of dye from the right was approximately 14 per cent in fifteen minutes. A plain roentgenogram was taken, followed by bilateral pyelogram. The right kidney appeared normal. The left kidney showed marked deformity. The ureter was tortuous and dilated, with marked clubbing of all the calyces and dilatation of the pelvis.

Operation was done December 10, 1936. The kidney was opened and found to be enlarged and hydronephrotic. On opening it, much foul pus was evacuated. The kidney had thinned out, but in this case, as in the first, there was still some structure left. A nephrostomy tube was inserted and irrigated at regular intervals. He remained in the hospital three weeks. The wound healed. He was rechecked March 17, 1937. The urine had cleared up. Catheters were passed to the pelvis of the left kidney without meeting any obstruction. Specimen collected showed only an occasional pus cell. Intravenous dye from the left side appeared in three minutes. The output was 12 per cent in fifteen minutes, showing remarkable recuperation of this kidney. The pyelogram showed it to have returned practically to normal. There is the delicate cupping of the calyces and no dilatation of the pelvis.

We have had other cases the results of which are quite similar to these.

SUMMARY

(1) Cases are shown illustrating the remarkable ability of the kidneys to undergo repair.

(2) Attention is called to the fact that a nonfunctioning kidney may not necessarily be a dead kidney.

(3) Stress is placed on the condition of the opposite kidney and the type of infection present in the involved kidney as prime factors in influencing the recovery of a badly damaged kidney.

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DISCUSSION (*Abstract*)

Dr. Geo. R. Livermore, Memphis, Tenn.—I think we are all in accord with Drs. Floyd and Pittman that the infected kidney or a kidney damaged by back pressure, is capable of a remarkable comeback.

In such cases, I agree too that Hinman's theory of renal counterbalance is not tenable. This comeback, I believe is a question of the amount of damage, the elimination of infection and complete removal of obstruction to the free flow of urine in the urinary tract.

In regard to rupture of the kidney, I am not in complete accord as I believe most of these cases demand exploration. The splendid work of Stirling and Lands, in the *Journal of Urology* for April, 1937, shows conclusively that failure to explore often means the death of the patient or at least the loss of the kidney. They state that a preliminary study in some cases may reveal little apparent injury when later we find the damage more serious, necessitating surgical intervention, and while the majority of such injuries may heal spontaneously, the kidney may become functionless later.

They cite four types of injury: (1) subcapsular ecchymosis and hemorrhage, surface contusions, and perivascular extravasation in perirenal tissues; (2) rupture of capsule, no laceration of parenchyma, as shown by no urinary extravasation; (3) laceration of parenchyma and transverse tearing of capsule; (4) laceration and pulping of parenchyma; kidney torn in two or three pieces or torn from pedicle.

They state *type 1* and *2* non-surgical, *type 3* surgical, with repair, and *type 4* nephrectomy.

Failure to explore may cause serious trouble and result in operation later.

STERILITY*

FROM THE VIEWPOINT OF THE GYNECOLOGIST

By CONRAD G. COLLINS, M.D., F.A.C.S.
and
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Sterility, though not dangerous to the lives of the individuals involved, may greatly influence their health, peace of mind, and happiness. The sociologic and economic aspects of sterility assume a formidable appearance when it is realized that many nations are apprehensive about their declining birth rates and many barren couples "are more or less maladjusted to each other as well as to life in general."[1] Sterility, without a doubt, is one of the foremost problems confronting the gynecologist today.

Sterility in its broadest sense means the inability of the female to conceive and deliver a viable fetus. In its strictest sense sterility is defined as "the inability to initiate the reproductive process."[1] Most authorities adhere to the latter view. Sterility, whether absolute or relative, primary or secondary, congenital or acquired, demands a thorough, painstaking and exhaustive history and physical examination of both partners.

As another essayist in this symposium will discuss sterility in the male, the authors will not discuss this aspect, aside from emphasizing that the male is a frequent contributor, in whole or part, to the unfruitful marriage.

In the history it is important to note whether or not the patient had mumps or scarlet fever when young. Of all the acute infectious diseases of childhood, these two are potentially most capable of injuring the gonads. A history of gonorrhea is important in that cervicitis and salpingitis, both frequent causes of sterility, are often found as a result of this disease.

The duration of marriage; whether or not the patient had been married before; the number of previous pregnancies, if any, should be recorded. Special note should be made as to the use of contraceptives; habits of intercourse; position assumed during intercourse; the presence or absence of dyspareunia; and whether or not the patient arises immediately after intercourse and goes to the bathroom to empty her bladder. Rubin[2] says that 77 of his sterile patients became pregnant simply by following the instruction of not urinating for several hours after intercourse. This is especially true in cases having extensive rectocele or birth injuries where effluvium seminis occurs as a result.

The patient's diet should be inquired into, as a lack of vitamin E in experimental animals definitely decreases their fertility. On the other hand, the use of vitamin E in sterile humans, to date, does not seem to be of much aid in establishing or aiding fertility. The excessive use of alcohol, tobacco or drugs should command attention, as these agents have been proven to decrease fertility. Occupation or overwork occasionally plays a part in a patient's inability to conceive. Of utmost importance is the menstrual history: the age of onset, frequency, duration, character, presence or absence of dysmenorrhea and whether or not there has been a change in the periods. The presence or absence of intermenstrual pain or periodic interval bleeding often gives an index as to the time of ovulation.

The physical examination should be complete, including the head, neck, thorax, abdomen and extremities. The height and weight should be recorded. Needless to say the pulse, respiration, blood pressure and temperature and hair distribution are noted. The amount and distribution of fat are important and anthropometric measurements should always be taken.

The pelvic examination should include a thorough examination of the external genitalia; vagina, cervix, uterus, and adnexa.

Laboratory work should include a blood, urine, stool and Wassermann examination. Basal metabolic rates and endometrial biopsy studies are imperative. Blood and urine determinations of hormones should be performed if facilities are available.

In examining the external genitals one should note the presence or absence of signs of infection

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*From the Department of Gynecology, Tulane University School of Medicine.

in Skene or Bartholin's glands, as often infection in these areas gives a clue to the possibility of gonorrheal invasion of the remainder of the genital tract. The hymen is carefully inspected as to rupture, rigidity or presence of painful carunculae. Infrequently after years of married life an unruptured or rigid hymen or painful carunculae myrtiformes are found which account for dyspareunia and consequent vaginismus, and preclude proper performance of the sex act.

The vagina is inspected by means of a speculum for evidence of infection such as is occasioned by yeast or trichomonas and wet and stained smears are made from any discharge which may be present. The discharge incident to the vaginitis is often detrimental to the viability of the sperm. Atresia, either congenital or acquired, of the vagina is occasionally encountered.

The cervix is inspected and areas of erosion or eversion are sought. Even more important is the presence of an endocervicitis accompanied by a thick mucous discharge or cervical plug, the latter often causing sterility in that it is mildly spermicidal and usually impervious to the passage of the sperm. A probe should be passed into the cervix in all cases and the presence or absence of cervical stricture determined. At the same time, by means of the probe, the length of the uterine cavity should be determined and recorded. Should an erosion and/or chronic endocervicitis be encountered, the infection should be eradicated by the judicious use of the cautery or conization electrode. For the infected cervix presenting eversion, proper methods of treatment should be instituted. If a stricture is encountered, dilatation should be performed.

The uterus is palpated and its size, shape, position and mobility are determined. One not infrequently finds an acutely flexed, small hypoplastic uterus. If this be the case and the patient fail to conceive in a few months on a more conservative regime, then surgery in the form of a dilatation, curettage and insertion of a glass stem pessary is advocated. Should the uterus be found to contain fibroids, myomectomy is the procedure of choice. Fibroids undoubtedly cause sterility and their removal is followed by a fair number of pregnancies. Miller and Tyrone,[3] in 1933, reported 128 cases of myomectomy followed by pregnancy in 33.3 per cent. If the uterus is found to be retrodisplaced and movable, it should be replaced manually and a Smith or Hodge pessary inserted. The pessary should be removed, cleaned and replaced every two months. Should conception occur, the pessary is left in place until the patient is four months pregnant and the uterus has risen from the true pelvis. This will greatly lessen the tendency for the patient to abort. Should a retrodisplaced fixed uterus be encountered, then operative suspension of the uterus is indicated.

Tubal disease is one of the most frequently encountered causes of sterility. As a result of inflammation, usually gonorrheal, sometimes nonspecific, the tubes become blocked, usually at the fimbriated extremity or cornu, or both. Even when the lumen of the tube is not completely blocked, the inflammatory reaction and its sequelae in the tubes may be enough to interfere seriously with tubal motility, which is important in the transportation of ova and sperm. Tubal patency is usually determined by insufflation of the tubes with air or carbon dioxide or x-ray visualization of a radiopaque medium. Once tubal closure has been definitely demonstrated, the chances of the patient's conceiving are very remote. Many operations have been devised to re-establish tubal patency; and some gynecologists even advocate suturing of the ovary in the cornu of the uterus where removal of all of the tube has been necessary. However, the results of these operations are very disappointing and the very remote chance that a patient has of becoming pregnant following them should be fully explained to her before operation is decided upon.

The ovaries are often the cause of sterility in that ovulation may not occur, even though the patient bleeds regularly. In cases of anovulatory menstruation the usual cause of lack of ovulation is failure of the ovary to respond to pituitary prolan or a lack of sufficient quantity of the latter to stimulate ovulation. In either case ovulation and subsequent corpora lutea formation fail to occur and the patient bleeds from an endometrium that is of a proliferative or even hyperplastic type. The latter types of endometrium in themselves are not conducive to the implantation and nourishment of the fertilized ovum. The same failure of ovulation may result when the ovary becomes surrounded by adhesions as a result of inflammatory disease, or should ovulation occur, the adhesions trap the ovum and fertilization is impossible. Not infrequently the prolapsed ovary, due to circulatory changes and consequent edema and congestion, undergoes cystic degeneration and ovulation ceases, the follicles reaching various stages of development, but never maturing. In

an attempt to aid or cause ovulation, pituitary and anterior pituitary-like hormones have been advocated. However, to date the results obtained by these hormones have been far from encouraging.

Of late, anterior pituitary-like hormone from the serum of pregnant mares has been shown in experimental animals to be the most powerful gonadotropic hormone yet discovered. Some clinicians are enthusiastic about the ability of this hormone to produce ovulation in the human being. However, it is too early properly to evaluate the use of pregnant mare's serum in cases of anovulatory sterility. The authors have used it in a few cases, but so far the results are inconclusive.

Thus far thyroid extract has been the most useful hormone that the authors have encountered in treating cases of sterility of endocrine origin. It is interesting to note that Winchester[4] recently showed that thyroidectomy in hens decreased egg production; and the administration of thyroxin to the same group restored egg production to 60 per cent of the normal control group. A more complete description of hormonal therapy in sterility will be given by another essayist in this Symposium.

Where an ovary is prolapsed and fixed by adhesions, laparotomy, freeing and suspension of the ovary are indicated, together with any other pelvic surgery needed. When a prolapsed ovary that has undergone cystic degeneration is encountered and some months' trial of hormonal therapy fails to aid or produce ovulation, then partial resection of the ovary is indicated.[5] One of us (C. G. C.) now has a total of four cases operated upon during the past ten years for cystic degeneration of both ovaries, causing menorrhagia. At the time of operation no evidence of ovulation or corpora lutea formation was observed. Partial resection of the ovaries in all cases resulted in a return of menstruation to normal. Subsequent pregnancies in these cases have proven that ovulation occurred following surgical procedure. X-ray to the pituitary and ovaries has been used in cases of anovulatory sterility with apparently good results.[6]

In all cases of sterility the Rubin test should be performed. If injections of air or carbon dioxide fail to convince one that the tubes are patent, then injection of a radiopaque medium into the uterus is imperative. The test is best performed between the tenth and sixteenth days of the menstrual cycle, which period, most authorities agree, is the probable time at which ovulation occurs. Should the tube prove patent it is a good plan to insufflate them regularly each month at or about the ovulation time until conception takes place.

No study of a case of sterility is complete without an endometrial biopsy. This simple office procedure gives much information as to the function of the ovary. The biopsy is usually taken on the twenty-sixth to the twenty-eighth day of the cycle. Should the endometrium obtained show secretory changes, ovulation and corpora lutea formation have taken place. However, should the endometrium show only the proliferative phase, then ovulation and corpora lutea formation have not occurred and anovulatory sterility is present.

If ovulation is proven by endometrial biopsy studies, then it is important to prescribe intercourse at or about the time of ovulation, for this period is most conducive to pregnancy. Most authorities agree that ovulation occurs between the tenth and sixteenth days of the menstrual cycle; and since the life of the ovum has been estimated as being two days, the importance of coitus during this time is evident. Unfortunately not all women ovulate between the tenth and sixteenth days. Rock[7] and co-workers have shown that the day of ovulation can be determined by means of a galvanometer of especial type. This apparatus at present is not available universally and most gynecologists must satisfy themselves with less accurate means. A method commonly used is palpation of the ovaries every day or so in an attempt to feel the growing follicle. Another is to have the patient take her temperature rectally every day, Zuck[8] stating that ovulation is accompanied by a drop in rectal temperature. Though the scientific accuracy of both of these methods might be criticized, they should be tried in every case of sterility until definitely proven to be of no value.

Many authorities recommend the use of the Huhner test, claiming that if numerous spermatozoa are found in the cervical secretion of the female any factor in the genital tract lower than the internal os can be eliminated as a possible

cause of sterility. An absence of viable sperms in the cervical secretion as well as the posterior fornix indicates that the cervix and vagina may both be at fault. Should motile sperm be found in the fornix but not in the cervix, then the cervix is one of the etiologic factors.

CONCLUSIONS

(1) In every case of sterility, the male should be considered sterile until proven otherwise.

(2) A detailed history and thorough physical examination should be obtained on all patients.

(3) Tubal patency in the female should be established by means of tubal insufflation and/or uterosalpingography.

(4) Dilatation of the cervix and therapeutic insufflation of the tubes at or about the time of ovulation should be carried out each month.

(5) The presence or absence of ovulation should be determined in each case by means of endometrial biopsy.

(6) Vaginitis or cervicitis, if present, should be eradicated by appropriate therapeutic means.

(7) Movable retrodisplacements should be treated by manual replacement of the uterus and insertion of a Smith or Hodge pessary. Fixed retrodisplacements should be treated by surgery.

(8) If fibroids are present they should be removed. Should an acutely antiflexed uterus be discovered, treatment by means of the stem pessary must be considered.

(9) Tubal reconstruction offers slight possibility of pregnancy. However, in selected cases it should be tried.

(10) In cases of sterility where anovulation is present, gonadotropic hormones and thyroid extract should be utilized. Failure of these agents to produce the desired result should bring to mind the possibilities of x-ray therapy and partial resection of the ovary.

(11) No operative procedure should be carried out on any woman until her husband has been proven, at least, relatively fertile.

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Discussion follows paper of Dr. Thomas, page 750.

STERILITY*

FROM THE VIEWPOINT OF THE UROLOGIST

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In dealing with sterility, the urologist is chiefly concerned with problems affecting the male. Fertility[1] is said to reach its peak when parents are about the same age, or when the husband is not more than six years older than the wife. It tends to diminish gradually after 33 in men and after 26 in women. The male is at fault in approximately 25 per cent of cases.

Sex cells are highly specialized and subject to disturbance by a wide variety of conditions. Tew[1] and others have shown that diseases upsetting the normal constitutional balance may be, and quite frequently are, associated with sterility. Notable among such diseases are typhoid fever, extragenital tuberculosis and syphilis. Exposure to x-ray, according to Huhner,[2] is a frequent cause of sterility. This is apparently true even when small doses are used in treating skin conditions in the genital region. Lead poisoning and chronic alcoholism, dietary deficiencies, worry and overwork are occasional etiologic factors. Sterility is produced by any of these conditions through its toxic effect upon the germinal epithelium, preventing the formation of spermatozoa. Impotence may also cause sterility.

Local conditions causing male sterility are numerous. They may involve the function of any part of the genital tract from the seminiferous tubules in the testicles to the fossa navicularis.

Among the testicular lesions are bilateral orchitis from mumps, gummata in late syphilis, undescended testicles, rarely injury, and more rarely temporary sterility from the toxic effects of an acute fulminating gonorrhea. An additional group of cases is encountered in which physical and laboratory findings give definite evidence of sterility, but no cause. Bothe and Robinson,[3] in studying a series of specimens, found histologic changes in the testes and epididymes which they felt could be the primary cause of sterility. In carrying out this study, they purposely eliminated all specimens showing gross changes. Undescended testes present a

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slightly different problem from other testicular lesions. Carl Moore[4] has shown that spermatogenesis is dependent upon the temperature regulating mechanism of the scrotum. Testicles within the abdominal cavity are exposed to a temperature appreciably higher than that within the scrotum and it is probable that this is a factor in causing degeneration of the germinal epithelium. It has also been shown that in the cryptorchid testes, in addition to the absence of germ cells, the interstitial cells are hypertrophied.

Obstruction in the epididymes from bilateral gonorrheal epididymitis is the commonest cause of sterility in men. From the operative findings of well over 200 cases, Hagner[5] stated that he found no involvement of the testicle itself, the epididymes and tunica vaginalis bearing the brunt of the infection. Another lesion of the epididymis is tuberculosis. It is confined to the epididymis at first, but spreads sooner or later to the testicle, and finally to the entire genital tract. Sterility in such cases is on both an obstructive and degenerative basis. Traumatic epididymitis is rarely if ever the cause of sterility. Malignancy is also rare.

The vas deferens may be involved along with the epididymis in gonorrheal infections, and it may suffer the same fate as a result of subsequent scar tissue formation. Huhner[6] calls attention to a very slight inflammation of the vas during gonorrhea which may produce no clinical evidence during the infection, but result in enough scar tissue formation to occlude the lumen. Obliterations of the vas from poorly performed varicocele and hernia operations are additional causes of male sterility.

Chronic infection of the prostate and seminal vesicles may alter the secretions of these organs so that they have a detrimental effect upon the viability of the spermatozoa. On the other hand, it is remarkable how much acute and chronic infection one sometimes encounters without any apparent effect upon fertility. I refer especially to those cases where pregnancy occurs in the presence of acute gonorrhea. Wolbarst calls attention to prostatitis secondary to influenzal infections of the respiratory tract. Whether or not such infection bears a relationship to sterility different from any other nonspecific prostatitis, I am unable to say. Sterility may also be produced by bands of scar tissue in the prostatic urethra which occlude the ejaculatory ducts.

Normally the urethra is a muscular tube which, during ejaculation, will expel the seminal fluid by a series of muscular contractions. Any condition interfering with this function will probably be associated with sterility. Haines[7] and others have made observations upon the sexual function of patients after suprapubic prostatectomy. The ejaculatory ducts empty into the urethra, which after operation is surrounded by inelastic fibrous walls. The semen in these cases remains in the prostatic urethra or trickles back into the bladder and is passed out with the next voided urine. Hurst[8] reported sterility in patients who had been subjected to presacral neurectomy. He stated that ejaculation is abolished, but potence and psychologic orgasm are not disturbed. The sexual function of women is apparently not affected by this operation.

Strictures of the urethra are rarely the cause of sterility. The canal would have to be almost completely occluded to prevent the semen from dribbling into the female genitals.

The two principal lesions of the penis which may cause sterility are the various grades of epispadias and hypospadias. The urethral opening in such cases may be situated in a position that will prevent the products of ejaculation from being deposited in the region of the cervical os. This is especially true in the penoscrotal and perineal types of hypospadias.

Endocrine disturbances are widely recognized at the present time as a cause of sterility. That subject, however, is fully discussed in another part of this symposium and will not be further considered here.

The diagnosis of male fertility is based primarily upon a study of the semen. One must be able to recognize specimens within the limits of normal and to correlate variations from the normal with clinical findings, in order to determine whether or not the male is at fault in a sterile marriage. Abstinence is advised for a period of 3 days prior to collection of the specimen. The powder on a condom is known to be detrimental to the viability of spermatozoa and should be carefully removed by washing before it is used. The ingredients of the rubber from which a condom is made may also be hostile and for that reason Hotchkiss[9] advises the use of a wide-mouth bottle. After collection the specimen should be kept at or below room temperature until delivered for examination. It has been shown that the temperature of a condom specimen can be reduced to freezing and motility restored by gradual thawing. Apparently then there is little danger in allowing the semen to get too cold while being transported to the ex-

aminer's office. On the other hand, spermatozoa are easily killed by heat that is appreciably above normal body temperature.

Human beings differ as individuals, and naturally, hard and fast rules cannot be applied to them. On that basis a certain amount of flexibility must be exercised in determining whether or not a specimen of semen is normal. The volume ejaculated ranges from 4 to 10 c. c. and contains four to five hundred million spermatozoa. Motility should be good and maintained for 24 to 36 hours at room temperature. At least 80 per cent of the cells should be normal forms. The reaction is alkaline, the pH ranging between 7.7 and 8.5. Reactions of 6.2 or less are thought to be responsible for necrospermia. Titus,[10] on the other hand, does not believe this to be an essential factor. Volumes of 0.5 c. c. or less are insufficient to protect the sensitive sperm. It has been repeatedly shown that if more than 20 per cent of the spermatozoa are abnormal, sterility is the result, or if pregnancy does occur it will end in miscarriage. If the semen is considered normal the male may be dismissed from further consideration. On the other hand, after examination of several interval specimens, if the semen is considered deficient, the male must be subjected to a more or less detailed study.

General debilitating diseases, lead poisoning, chronic alcoholism, and so on, are usually self-evident and require no special discussion. A routine blood Wassermann should be done in order to safeguard against the possible part that syphilis may play. The sex life of the individual should be carefully investigated, as sexual excesses and abnormal sex practices have been known to account for sterility.

Testicles that are grossly normal as regards consistence are, in the majority of cases, physiologically normal also. Size does not constitute abnormality, as extremely small testicles may be capable of perfectly normal spermatogenesis. Gross degenerative lesions are not often hard to recognize.

Obstructive lesions of the genital tract are most commonly situated in the epididymes. A history of bilateral epididymitis, combined with nodular induration in the lower poles, is strong presumptive evidence that the trouble is at this point.

Obstruction in the distal segments of the vasa are unusual. When such lesions are suspected the scrotal segments may be exposed and injected with colored solution. If the solution appears in the urethra or is later expressed from the vesicles, the lumen is patulous.

Chronic infections of the prostate and seminal vesicles are determined by examination of secretions obtained after massage. In addition to the usual study of the wet slide, a stained specimen should be examined in an effort to determine the type of infection present.

Obstruction in the ejaculatory ducts may be discovered by endoscopic catheterization. This procedure, however, is probably of more academic interest than of practical importance in the management of sterility.

Urethral stricture and congenital deformities are easily recognized. The only problem is to determine whether or not the condition present is sufficient to produce sterility.

Prognosis.—Read,[11] in a study of 1,000 males who were partners in sterile marriages, stated that about 30 per cent were curable. This is approximately the figure reported by other investigators.

Treatment of the male has for its aims the production of a normal semen and the correction of any abnormalities that might interfere with normal genital function. It may be necessary to rebuild health by correction of dietary deficiencies, occupation, and especially sex habits. Alcohol has a devitalizing effect upon spermatozoa and should be omitted in cases where its use is associated with sterility. When the cause of sterility can be assigned to syphilis, good results may be expected from antiluetic therapy. Hagner[12] reported a case of bilateral testicular gummata in which spermatogenesis was restored by treatment.

Chronic infections of the genital tract should be cleared up, but the patient should be made to understand that this treatment may not correct his sterility. We have a few records in our files, however, in which this did occur. One case worthy of note was that of a man 45 with a

rather long-standing prostatitis. His wife had not been pregnant for sixteen years and no contraceptive measures had been used. Pregnancy occurred within six months after the infection was cleared up. Dilatation of urethral strictures improves drainage and facilitates the cure of infections in the prostate and seminal vesicles.

The treatment of undescended testicles has been modified somewhat during the past few years. At the present time it is thought that normal descent is due to a substance produced in the anterior lobe of the pituitary gland. In the case of cryptorchids this substance is supposed to be deficient. On that basis, the hormone has been administered in the form of anterior pituitary-like sex hormone over variable periods. The best results have been obtained at or before puberty, but it may be of value after that. On the other hand, an increased activity of the pituitary at puberty is thought to account for a few cases that descend without treatment at that time.

Of the operative procedures suggested for undescended testicles, the one devised by Torek has been most satisfactory in our hands. For detail as to technic, I refer you to articles by him on that subject. The majority of cases are operated upon between the ages of 6 and 10 years, with a tendency at the present time to operate at the earlier ages. In bilateral cases one side is done at a time. Spermatogenesis may be restored by operation long after puberty. Torek himself reported a good result in a patient 38 years old. In view of our present knowledge, anterior pituitary-like sex hormone should be administered first, and only those cases that fail to respond to it should be subjected to surgery.

Sterility following bilateral gonorrheal epididymitis is due to an occlusion of the efferent duct in the globus minor. It may be overcome in some cases by anastomosis of the vas to the globus major of the epididymes. This operation was first suggested by Edward Martin and later modified by Hagner and others. There are two conditions, according to Hagner,[13] that must be present for a successful result in this type of sterility:

"First, the vas must be patulous above the point of anastomosis; and second, the globus major, or the upper portion of the body of the epididymis, must contain live spermatozoa."

He emphasizes the importance of using silver wire sutures in making the anastomosis, and points out that his only successful cases were those in which it was used. The globus major is chosen as the site for anastomosis because its efferent ducts are numerous, a point favoring the possibility of obtaining an open channel. In cases that are carefully selected for operation, approximately 60 per cent of cures are reported.

Epispadias or the hypospadias of sufficient degree to produce sterility, can be corrected only by surgery. The urethra is reconstructed with the meatus placed as nearly as possible in its normal position. I recently saw a case of complete epispadias upon which Dr. Rudolph Matas had done a plastic repair 37 years before. The patient had a partial incontinence of urine, but the urethra was complete and the meatus was in the end of the penis. The patient has two children, and sexual performance has always been satisfactory.

SUMMARY

Sterility in the male may present a rather complicated problem.

All possible etiologic factors should be given careful consideration.

The semen and genital tract require a detailed study.

When the cause of sterility is established, the indications for treatment are usually quite clear.

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Discussion follows paper of Dr. Thomas, page 750.

STERILITY*

FROM THE VIEWPOINT OF THE ENDOCRINOLOGIST

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In 1889, Brown-Sequard announced to an incredulous and taunting Societé de Biologie that he had been invigorated by the daily ingestion of testicular press-juice, and established himself as the first recipient of substitutional hormonal therapy. Claims and counter claims for the effectiveness of this medication stimulated investigative study and, through the subsequent years, to these first observations of Brown-Sequard, physiologists, first motivated by disbelief and later captured by the romance of this adventure and encouraged by the discovery of previously unknown facts, have added an increasing volume of experimental data, until, at the present day, the literature of experimental and clinical endocrinology threatens to exceed, in bulk and confusion, the enormous body of written matter which has collected upon the subject of neoplastic growths.

When hormonal substances of uncertain action and less known strength became available, the physician clamored for their use in the treatment of his patients. To pacify this turmoil, and with permissible regard for their own interests, pharmaceutical houses began to market powders and solutions of every known organ in the body, singly and in combination, for clinical use. Most of these preparations with the notable exception of desiccated thyroid substance and preparations of the adrenal gland were inactive and useless, but none the less popular. These gland substances were given by mouth and enthusiastic reports concerning their value cluttered the literature despite the fact that there was no sound basis underlying their use and no proof of their effectiveness. Knowledge of endocrine function was still vague and indefinite, and physiologists were handicapped by their failure to isolate the active products of gland secretions.

The discovery by Smith and Engle, and by Aschheim and Zondek, of an active pituitary-like hormone in the urine of pregnant animals, and the discovery of crystalline estrone by Butenandt and Doisy, and of crystalline progesterone by Butenandt and Allen, all accomplished within the last fifteen years, increased the effectiveness of experimental investigations which, in the last few years, have resulted in the organization and assimilation of a previous mass of confusing and contradictory data into a comprehensible outline of endocrine function.[1] The isolation of these relatively pure products has also paved the way for the commercial production and clinical use of effective and standardized hormonal preparations, rather unstable in character but possessing specific actions.

Our knowledge of the reproductive process and of the functions of the various reproductive organs in experimental animals of both sexes, revealed by endocrine investigation, has increased tremendously. Limited investigation of the human species, aided by analogies revealed in comparable animal research, and sustained in part by assumptions and hypotheses, has provided a well-supported conception of the nature and mechanism of spermatogenesis, oogenesis, menstruation, ovulation, fertilization, and pregnancy, and has furnished to the profession a clearer understanding of the functional abnormalities which may disturb these processes. But let it not be forgotten that while our knowledge of these processes in the animal is, to some extent, positive and confirmed, our knowledge of these same functions in the human is, to a great extent, presumptive and based largely upon assumption, hypothesis, and analogy.

Before the endocrinologic aspects of sterility can be discussed, it is necessary that the normal physiology of those endocrine glands, which are chiefly concerned in conception, be reviewed and that the commoner abnormalities to which they are liable be considered.

From the great mass of collected endocrine data, certain generalizations can be made concerning the function of the reproductive organs. It seems apparent that the two gonadotropic hormones of the anterior pituitary gland definitely control and regulate the activity and function of the gonads in both sexes. These two hormones are termed, because of their function in the female, the follicle stimulating hormone and the luteinizing hormone. There is no apparent qualitative difference between the gonadotropic hormones of the male pituitary and the female pituitary, although quantitative differences have been described.

In the female, the follicle stimulating hormone

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provokes the growth, development and maturation of the primordial follicle into the graafian follicle. The luteinizing hormone converts the granulosa cells of the follicle into lutein cells and causes the transformation of the ruptured follicle into a corpus luteum. Ovulation, or rupture of the follicle, seems to be dependent upon the combined action of both of these substances, since ovulation has been produced in experimental animals, including the monkey, by injections of these substances in a rough proportion of fifty parts of follicle stimulating hormone to one part of luteinizing hormone.

In the male, the follicle stimulating hormone causes the development of the semeniferous tubules which are responsible for spermatogenesis. In the experimental animal, the administration of this hormone will provoke tubular repair and cause the resumption of spermatogenesis even when tubular atrophy has been produced by hypophysectomy. The luteinizing hormone stimulates the growth and hypertrophy of the interstitial tissue of the testis.

Properly stimulated by the pituitary, the gonads themselves produce hormones which, in turn, affect the accessory organs of reproduction such as the tubes, uterus, cervix, vagina, in the female, and the penis, prostate, seminal vesicles and scrotum in the male. In addition, these gonadal hormones also exert an effect upon the anterior portion of the pituitary gland.

In the female, the developing follicle secretes an estrogenic hormone which, among other actions, produces growth, proliferation, and increased vascularity of the endometrium. This substance is responsible for the repair of the endometrium following menstruation. When the corpus luteum is formed, this structure also begins to elaborate the estrogenic hormone, so that endometrial growth continues, but the corpus luteum secretes, in addition, a second hormone, termed progesterone, which causes a secretory activity in the endometrial glands. This secretory activity is first manifested by an elongation of the epithelial cells of the surface membrane and necks of the glands. Beginning in the surface portion of the endometrium, it gradually progresses towards the base. The nuclei of the secretory cells retreat from the basement membrane. The increase in size of the cells causes them to project forward into the lumen of the glands, imparting to these structures a coiled, corkscrew-like appearance. This secretory activity of the endometrium, resulting from corpus luteum stimulation, is termed the progestational phase because it has been found necessary for the endometrium to be prepared in this manner if implantation is to occur, and it is only under these circumstances that this tissue offers a favorable environment for the nidation of the ovum. In contrast, the endometrium which is under the stimulus of estrogen alone is termed a proliferative endometrium. Accordingly, the menstrual cycle can be divided into a follicular phase, during which the endometrium is in a state of proliferation, and into a luteal phase, dependent upon corpus luteum formation, during which the endometrium is in a state of secretory activity. An early and a late stage of both the proliferative and the progestational endometrium can be recognized, depending upon the duration of the follicular or the corpus luteum stimulation.

The cyclic phenomenon of menstruation is explained by the effect which estrogen and progesterone have been demonstrated to exert upon the gonadotropic hormones of the pituitary. Estrogen, in certain concentrations, inhibits, or depresses, the follicle stimulating hormone and simultaneously stimulates, or increases, the secretion of luteinizing hormone. Progesterone inhibits the luteinizing hormone. The correlation of these facts indicates that during the follicular phase of menstruation the follicles, under the stimulation of follicle stimulating hormone, grow and develop, and secrete increasing quantities of estrogen which gradually suppress the follicle stimulating hormone and stimulate the production of luteinizing hormone. In addition, estrogen produces a proliferative phase of the endometrium. The proper proportions of follicle stimulating hormone and luteinizing hormone produce ovulation, following which the follicle stimulating hormone becomes suppressed. The increasing production of luteinizing hormone causes the luteinization of the ruptured follicle which now begins to elaborate progesterone which, in turn, provokes the progestational phase of the endometrium. Increasing concentrations of progesterone inhibit the luteinizing hormone so that the stimulus which maintains the corpus luteum is lost, and this structure degenerates and ceases to produce estrogen and progesterone. Menstruation follows the degeneration of the corpus luteum, follicle stimulating hormone is again produced by the pituitary, and the cycle commences all over again.

In the female, it appears that estrogen and progesterone act synergistically, and in sequence, upon the accessory sexual organs and also upon

the pituitary gonadotropic hormones. In turn, the gonadotropic hormones act synergistically upon the ovaries. While it is true that the ovaries are governed and controlled by the pituitary, it seems equally true that the pituitary is governed, in large part, by ovarian activity, and that the gonads do possess, in this indirect manner, some degree of self-regulation.

In the male, only one testicular hormone has, at present, been revealed. This substance, which can be termed androgen, exerts a stimulating action upon the male accessory organs in a manner comparable to the effect of estrogen upon the female accessory organs. It also inhibits or suppresses the follicle stimulating hormone and it possesses no direct action upon the gonad itself. No cyclic function has been demonstrated in man, although, in lower vertebrates, there is a definite periodicity in male sexual function.

Although the pituitary and the gonads are the glands which are primarily concerned in sexual function and reproduction, experimental and clinical data reveal the fact that the proper quantitative and qualitative balance between the hormone secretions of these two structures, essential for normal function, is greatly altered and affected by disturbances in other endocrine organs, notably the thyroid, the pancreas, and the adrenals. While our knowledge concerning the influence of these organs upon the pituitary-gonad relationship is meager and obscure, it would appear that such an effect is exerted chiefly through the pituitary. The clinical effect which has been noted in sterility and menstrual disturbances from both hypofunction and hyperfunction of the thyroid gland is well known. The effect of diabetes and other disturbances of sugar metabolism is equally familiar, but the relationship is more vague. While marked alterations in sexual function have been noted in abnormalities of the adrenal glands, our knowledge of the physiology of these organs is incomplete, and their influence upon sexual physiology is still a matter of conjecture.

While cyclic uterine bleeding is usually associated with ovulation and the formation of a corpus luteum, it is now known that bleeding may occur without ovulation. This bleeding, termed pseudomenstruation or anovulatory menstruation, may be either cyclic or acyclic in character. It is usually characterized by an increase in the profuseness of the flow and by an irregularity in the cycle, although, in many instances, the bleeding is normal in amount and the periods are regular in their appearance. Biopsies of the endometrium, during the period of bleeding, reveal that the endometrium is always in a proliferative phase and is characterized by a complete absence of progestational reaction. Ovulation does not occur and the bleeding results from this proliferative endometrium because of a sudden lowering of the estrogenic stimulus. The microscopic appearance of the endometrium, in cases of anovulatory menstruation, depends upon its quantitative stimulation with estrogen. If the tissue has been subjected to prolonged, excessive estrogenic action, the picture will be that of the "Swiss cheese" pattern, in which the endometrium is markedly hypertrophied and the glands are dilated and cystic. If the estrogenic stimulation has not been excessive, the endometrium will be found in either an early or late proliferative stage. If the estrogenic stimulation has been particularly weak, the endometrium will be found atrophic in character.

Corner has demonstrated the frequency of the anovulatory menstrual cycle in the monkey, and clinical studies of the human indicate that it is commonly encountered in gynecologic practice. Lass, Smelzer, and Kurzrok studied the frequency of anovulatory cycles in forty-seven lactating women who had a regular menstrual periodicity. These investigators reported that 55 per cent of 196 cycles were anovulatory. While the character of the endometrium is necessarily dependent upon abnormalities of ovarian function in anovulatory menstruation, the primary cause of the condition is still unknown. It is possible that the endometrium simply reflects a disturbance of the pituitary-gonad relationship which might be caused by either deficient stimulation of the ovaries by the pituitary, or by deficient stimulation of the pituitary by the ovaries. It is also possible, but improbable, that the disturbance may represent a primary abnormality of the endometrium in that this tissue cannot properly metabolize the normal ovarian hormones. Again, it is possible that the disturbance may lie primarily in some other endocrine organ and that the anovulatory bleeding is but the reflection of this extraneous factor upon the pituitary-gonadal balance.

In monkeys, it is well known that many of the cycles are anovulatory and that many of them are ovulatory, and that the animal for no apparent cause or reason will change from one to the other. It is reasonable to assume that anovulatory menstruation in the human is only temporary in nature and that the disturbance may

spontaneously correct itself at various times throughout the woman's life.

Aside from the disturbances which are presented, in the female, by anovulatory menstruation, disturbances may also occur in the ovulatory cycle. Occasionally, an endometrium is seen which, though in a definitely progestational phase, exhibits only a limited and not a full secretory response. Ovulation occurs in such instances and a corpus luteum is present, but its function, gauged by the endometrium, is judged to be deficient. In rare instances, an endometrium can be found in which there is a full progestational response, in scattered portions, associated with some degree of cystic changes in the glands. This endometrium has been proven, by Kurzrok, to result from excessive stimulation with estrogen before the occurrence of ovulation, and consequently, a progestational reaction becomes superimposed upon a cystic endometrium.

Functional disturbances of the sexual organs may also occur in the male, but our knowledge of these conditions, unfortunately, is limited. It is definitely known that a complete loss of pituitary stimulation upon the testis will result in a complete absence of spermatozoa, and it is possible that lesser disturbances may be sufficient to cause either a decreased number of sperm, or else abnormalities in sperm morphology. Cryptorchidism, a definite endocrine stigma in itself, further exposes the testicle to an injurious thermal environment and can be responsible for either a complete absence of spermatozoa, or else for abnormalities which render the sperm infertile.

In discussing the relationship of endocrine disturbances to sterility, it is necessary that both the male and the female be considered; and it is also necessary that the progress of events which transpire in normal conception be reviewed, and the effect which endocrine dysfunction may have upon these processes be described.

In order for conception to occur, it is necessary that a female be inseminated with healthy, motile spermatozoa which are capable of fertilizing the ovum. It is further necessary that the spermatozoa gain entrance into the cervix, be afforded a favorable environment, be permitted, or even helped, to ascend the uterus and meet and fertilize the ovum in the fallopian tube; it is then necessary that the fertilized ovum be transported through the tube and become implanted in the uterus. From a practical point of view, these problems can be grouped into: (1) abnormalities of the spermatozoa; (2) abnormalities in transportation of the sperm; (3) abnormalities in the ova; (4) abnormalities in transportation of the fertilized egg; (5) abnormalities in implantation.

In the female, the process of transportation of the sperm and of the fertilized eggs has been shown, in experimental animals, to be partly, if not altogether, under the control of the ovarian hormones. However, our knowledge of this problem is still vague and obscure and it is assumed, if the endocrine status of the individual is in a state of function sufficient to meet the requirements of ovulation and implantation, that the question of adequate transportation for both the sperm and the ova will be well answered. If this assumption be made, the problem of sterility narrows down into a consideration of abnormalities in spermatogenesis, abnormalities in ovulation, and abnormalities of implantation.

In the examination of the male, all evident endocrine stigmata should be noted, but interest is centered chiefly upon the character, number, morphology, and motility of the sperm as revealed by the examination of a condom specimen. If abnormalities are found in this specimen, the male should be referred for a complete urologic study in order that organic disease may be excluded as a cause. If no organic lesion is found, or suspected, it can be assumed, provided that there are definite clinical stigmata of endocrine dysfunction, that the deficient spermatogenesis is endocrine in origin. In such instances, injections of both the follicle stimulating hormone and the luteinizing hormone may be used in an attempt to stimulate spermatogenesis in the tubules and the production of androgen in the interstitial tissue of the testis.

There are several commercial preparations of the follicle stimulating hormone which are prepared by extraction of the animal pituitary.* Variations in the standardization of these products make comparison difficult. Regardless of the preparation used, injections of at least 300 rat units should be given three times weekly for three weeks.

The luteinizing hormones on the commercial market are all derived from pregnancy urine and are usually termed anterior pituitary-like hormones, or chorionic gonadotropic hormones. These substances possess no follicle stimulating

*Among these are "gonadotropic factor" (Ayerst, McKenna & Harrison), "antuitrin" (Parke, Davis), "gynantrin" (Searle), "prephysin" (Chapel), and many others.

activity and differ in this respect from the true prepituitary preparations.*

Injections of this substance, in doses of from 200 to 400 rat units, should be given at the same time and at the same intervals as the doses of the follicle stimulating hormone.

After three weeks of such therapy, the patient should be given a rest of from three to four weeks, at the expiration of which time treatment should be resumed as previously. Not more than three or four such series of injections should be given.

Recently, preparations of a gonadotropic factor derived from the serum of pregnant mares have become available. Experimental investigations of the action of this substance in animals, and the results of fractionation of the mare serum, reveal that it appears to be both follicle stimulating and luteinizing in action. Accordingly, this substance may be used in place of a follicle stimulating hormone or, if desired, it may be used to replace the combined injections of the follicle stimulating hormone and the luteinizing hormone.†

Several reported instances can be found in the literature where such therapy has apparently increased the sperm count, when the count was low, but no success has ever resulted, to my knowledge, in the re-establishment of spermatogenesis, by endocrine therapy, in cases of azoospermia. While the re-establishment of spermatogenesis in hypophysectomized animals, following the injection of follicle stimulating hormones, is encouraging, it must be admitted that the results of endocrine therapy in the male have been extremely unsatisfactory and discouraging.

The examination of the female patient in the study of sterility presents three chief points of great importance when viewed in the light of possible endocrine therapy. These are the presence of underdevelopment and infantilism of the genital structures, the occurrence of ovulation, and the exhibition of a full progestational response by the endometrium. Infantilism is frequently associated either with amenorrhea or with anovulatory menstruation, but, in some instances, perfectly normal ovulatory bleeding occurs from a uterus which exhibits mild degrees of underdevelopment. It is likely that any influence upon sterility, which infantilism may exert, is related to amenorrhea or anovulatory menstruation. Ovulation is, of course, essential to fertility and requires no discussion regarding the part it plays in conception. While a full progestational response in the endometrium is usually associated with ovulation, it has been shown that, in some instances, the response is not maximal and, consequently, the endometrium does not afford a favorable environment for nidation of the ovum.

Infantilism in the genital structures is determined by the findings of the vaginal examination and by the measurement of the uterine index. The distance from the external os to the top of the fundal cavity, and the distance from the external os to the internal os, is measured with a uterine sound and the relationship between the length of the fundus and the length of the cervical canal is noted. The uterine index is expressed as one-half of the quotient obtained by dividing the distance from the internal os to the fundus by the distance from the external os to the internal os. Normally, this factor should be 0.75 or greater; in infantilism, the uterine index is 0.60 or less.

Infantilism is best treated by injections of the follicle stimulating hormone. This substance can be administered in a dose of 200 units three times weekly for a period of from four to six weeks. The response of the ovaries to such therapy can be checked by the determination, upon vaginal examination, of an increasing size of the uterus, by cornification of the vaginal mucous membrane, and by the response of the endometrium obtained by biopsy. If the response is satisfactory, as judged by an estrogenic effect upon the genital organs, injections of a luteinizing hormone may be used for a period of two to three weeks. All therapy should then be stopped and the patient should be given a rest so that the danger of creating a refractory state in the ovary, by injections of gonadotropes, may be eliminated. If normal menstruation, or if satisfactory growth, does not take place within a period of six weeks to two months, treatment may be resumed in a similar fashion. Excessive treatment, in an attempt to overstimulate the gonads, should be avoided. If the response, after three series of such injections as outlined above, is unsatisfactory, this form of therapy is best abandoned. Definite growth may be provoked in the genital organs by injections of an estrogenic substance, and attempts at ovarian stimulation by gonadotropes can be resumed

*The most commonly known are "antuitrin-S" (Parke, Davis), "A. P. L." (Ayerst, McKenna & Harrison), "follutein" (Squibb), "korotron" (Winthrop), and "pranturon" (Schering).

†Preparations, which are obtainable on the commercial market, are represented by "gonadin" (Cutter), "gonadogen" (Upjohn), and "anteron" (Schering).

after a sufficient estrogenic response has been elicited.

The occurrence of ovulation, and of a full progestational response of the endometrium, can be determined by a biopsy of the endometrium. This procedure is easily performed without an anesthetic and causes but slight discomfort. Any of the special instruments devised for this purpose may be used, but it is my personal opinion that none of these serves the purpose as well as a No. 1 sharp Sims curette. The biopsy specimen, to be used in the study of sterility, should be obtained within the first ten hours of the menstrual flow.

Endometrial activity, determined by microscopic examination, reveals, qualitatively and quantitatively, the hormonal stimulation exerted by the ovaries. Some idea, in an indirect manner, is also afforded of pituitary function.

If the endometrium is found to present a full progestational response, it can be assumed that ovulation is occurring normally and that the endometrium affords a satisfactory environment for implantation of the ovum. If the endometrium exhibits a progestational response that is limited, and not complete, it can be assumed that ovulation occurs, but that the corpus luteum function is deficient, and the endometrium, consequently, does not afford a favorable environment for implantation. This constitutes what is termed ovarian failure of the first degree. If the endometrium shows no progestational response, but exhibits evidences of a normal, or an excessive, estrogenic proliferation, it can be assumed that no corpus luteum is formed and that ovulation has not occurred. This functional state is termed ovarian failure of the second degree. If only a weak estrogenic proliferation, or if an atrophy, is found in the endometrium, it can be assumed that follicular development in the ovary is decreased. Such an occurrence is termed ovarian failure of the third degree.

Since ovarian failure of the first degree is characterized by the occurrence of ovulation, but a deficiency in the corpus luteum, it is rational to treat this condition with the injection of luteinizing hormones alone. Since it is also known that estrogen stimulates the production, by the pituitary, of the luteinizing hormone, and since it is possible that the deficient progestational response is caused by insufficient priming of the endometrium rather than by deficient corpus luteum function, the addition of estrogenic injections is a reasonable adjuvant. A suitable estrogenic preparation should be administered at approximately the expected date of ovulation. A dosage of 10,000 to 25,000 units is advised. Injections of the luteinizing hormone, in a dose of 200 units, should be instituted several days after the expected date of ovulation and should be continued every third day. Three such injections are usually sufficient.

Ovarian failure of the second degree is associated with anovulatory bleeding. Therapy should aim at the production of ovulation and the formation of a corpus luteum. This should be attempted by injections of the follicle stimulating hormone over a period of several weeks, followed by the injections of a luteinizing hormone. Hamblen[2] has demonstrated the futility of therapy with the luteinizing hormone alone. Since ovulation, in the monkey, can be produced by proper stimulation of the follicles by subcutaneous injections of a follicle stimulating hormone, followed by the intravenous injection of this same hormone, or else by the injection of a proper combination of both the follicle stimulating and luteinizing hormones, the attempted production of ovulation in the human would hold more promise if similar methods were used. The reported successes of Davis and Koff[3] are encouraging. However, it should be remembered that the cases in which ovulation was produced exhibited no evidences of previous ovulatory disturbances. It is significant that three of the patients, in whom the endometrium was cystic, presented no evidences whatsoever of ovulation or of corpus luteum formation. No one has ever yet proven the production of ovulation, provoked by endocrine therapy, in the human who previously exhibited an anovulatory cycle. The use of pregnant mare serum, as a follicle stimulating agent and as a stimulant to ovulation, followed by injections of a luteinizing substance, seems to offer the best hope of producing a normal ovulation and corpus luteum formation in the human subject.

Ovarian failure of the third degree is usually associated with infantilism, but is sometimes found associated with anovulatory bleeding. Its treatment follows the lines of therapy which have been advocated for the treatment of infantilism or for the treatment of ovarian failure of the second degree.

While concern is shown chiefly in disturbances of the pituitary gonadal balance as a causative factor in the production of sterility, disturbances in other endocrine organs should not be neg-

lected. Of these the commonest is hypothyroidism. The influence which the thyroid hormone produces upon conception is not definitely known, but the clinical relationship which hypothyroidism bears to sterility, miscarriage, and habitual abortion was recognized long ago. Brilliant results in the treatment of sterility in the hypothyroid woman accompany the exhibition of this substance in proper doses. In the absence of clinical evidences of hypothyroidism, and with a normal basal metabolic rate, the average woman appears to be benefited by this medication. When used empirically, the initial dose should be small and the drug should be periodically increased until its desired effects are obtained. The use of this drug in ¼ grain doses, three times daily, provided it does not produce evidences of toxicity, is of unquestioned value in the treatment of any case of sterility of endocrine origin.

An evaluation of the results which can be expected from endocrine therapy in the treatment of sterility is most discouraging. In those cases where ovarian failure of the first degree is the apparent causative factor, the results are very satisfactory, but in those instances in which a failure of ovulation is associated with infertility, but little hope can be held for relief from endocrine therapy alone. It is possible that what little success can be claimed for therapy in this condition is in reality a result of the patient's own spontaneous solution of her own endocrine difficulties.

In reviewing eighty-three cases of sterility that have occurred during the last three years, in the private practice of Dr. Hilliard Miller, with whom I am associated, and myself, I find that excluding those cases which resulted from azoospermia in the male, or from a complete obstruction of the fallopian tubes in the female, relief was obtained in over 65 per cent of the cases. In no single instance can a successful outcome be attributed to endocrine therapy, except from the use of desiccated thyroid gland.

While the success of endocrine therapy in the treatment of sterility holds but little promise at the present time, there is every reason to expect that, with an increasing knowledge of the normal processes of sexual physiology and conception, and with the help of more potent and more economical hormonal substances, successes from glandular therapy will become more frequent and the dreams of its pioneer investigators will be realized.

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DISCUSSION (*Abstract*)

Symposium on Sterility, papers of Drs. Collins and Miller, Dr. Burns and Dr. Thomas.

Dr. Robert E. Seibels, Columbia, S. C.—I became from the beginning rather conservative in surgical practice, probably due to an incident that happened quite early in my career. I was sitting in the office, waiting and hoping that a patient would come in. A very large and prosperous colored woman came in, starched skirts, apron and all. You could sort of see the fibroid, don't you know? There was at least $10. She sat down and I said: "What can I do for you, Auntie?"

"Is you the Doctor?"

"Oh, yes."

"Is you a surgical doctor or a medical doctor?"

"I am a surgical doctor, a very experienced surgeon. I have had lots of experience. I am one of the best surgeons you ever heard of."

"Do you cut people with a sharp knife?"

"Oh, yes, we use a knife very successfully."

"Well, great God, you ain't the doctor I'm looking for."

So my lack of conservatism cost me my entire private practice, and I think that was a valuable lesson.

I certainly am conservative when I advise a patient to have any sort of operation for the relief of sterility. In fact, I do not do it unless the lesion for which I am going to operate is of significance to the patient, is a pathologic condition. I think that we are inviting trouble for ourselves and our patients when we operate upon them so that they may become pregnant. That is, perhaps, ultra conservatism.

I have seen two patients have a fulminating pelvic peritonitis with a frozen pelvis as a result of artificial insemination at the hands of most competent gynecologists. I do not say that will occur often, perhaps, but we must keep its possibility in mind.

In this particular field one is more likely to be led astray by false reasoning than in almost any realm of treatment. I recall a patient who came to me at the age of 41, in her first pregnancy. As she rather reasonably put it, for the previous ten years she had been "share-cropped" through the entire medical profession and had given up hope five years ago and now she was pregnant. If I had been the last doctor who treated her, I, of course, would have claimed the credit.

Dr. E. C. Hamblen, Durham, N. C.—I should like to comment briefly on a very limited phase of this subject, that of therapy with the so-called "gonadal stimulators," the gonadotropins. There has been a general disappointment, I believe, in the therapeutic accomplishments of the chorionic (pregnancy-urine) and pituitary gonadotropins, but during the past year considerable optimism and enthusiasm have developed concerning the equine (mare's serum) gonadotropins.

In both the endocrine sterility of the male and female

our results have been very poor with these gonadotropins. In a series of 8 males with oligospermia, and consequent sterile mating, who have been intensively treated during the past year or so with all types of gonadotropins, singly or in combination, there was a uniform failure of therapy to produce any increase in the number of spermatozoa in their seminal fluids. Most spermatic counts grew lower as treatment was intensified or continued. This seemed particularly true when the equine gonadotropins were employed.

Our results with the various gonadotropins have been poor in the treatment of ovarian sterility of the female. Even the equine gonadotropins have salvaged few pregnancies for us in women whose uterine bleeding occurred from estrogenic endometria. We believe that in the majority of these women the primary pathologic condition is an ovarian refractivity to the gonadotropic influences of the pituitary gland. If such an ovarian refractivity exists, one should not expect to overcome it by giving more stimulation. Nature frequently has already tried this by inducing compensatory hyperfunction of the pituitary. In a certain group of women, the ovarian sterility may be due to inadequate gonadotropic stimulation by the pituitary. Here, equine gonadotropins may supply a deficit if given and, thereby, may permit the induction of normal ovarian responses which may result in pregnancy.

One may not be able to assess the receptivity of ovaries without carrying out a therapeutic trial of equine gonadotropins. I feel that women with proven endocrine sterility should be given such a test of therapy, but I see no justification for giving every sterile or presumed sterile female injections of equine gonadotropins as the first move, before any sensible diagnostic regime has been initiated. There is too much of this type of so called endocrine therapy practiced. Dr. Thomas has described for you in detail the methods of carrying out such a therapeutic test.

In our enthusiasm for the new, we should not forget the old. Mild degrees of hypothyroidism, not suspected clinically or diagnosable by metabolic studies, may produce a marked lowering of fertility. Every sterile woman, in whom no organic cause is apparent, should be given a therapeutic trial of thyroid substance. More pregnancies can be salvaged in patients with presumed endocrine sterility from adequate therapy with thyroid substance than from the routine use of equine gonadotropins.

Dr. Charles Edwin Galloway, Evanston, Ill.—If a woman comes in and says that she would like us to see why she does not have a baby, we hand her a card on which is written all of the various tests that we make, ten or twelve of them at least, and we say to her: "Here is the way in which we try to find out whether or not you will conceive. It calls for the cooperation of your husband as well as of yourself, and we will not handle your case unless both of you are perfectly willing to go through with all of these tests." We tell her about what it will cost her and that she must be ready to face the investigation, that she is not coming for an examination, but for an investigation of sterility.

If she is unwilling to do that and if her husband is unwilling to do that, we do not care to handle the case, because if you examine a woman, time after time she will walk out of your office and tell her friends that you said that she could not be pregnant, regardless of whether or not you said anything. I think it is a good idea, if you are going to handle a case of sterility, to undertake it on the proper basis at the beginning.

The patient should be told that if she has been married for three years and has not become pregnant, her success will range around 15 to 20 per cent. She should be told that before she begins to spend her money on various laboratory tests, so-called "shots," and so on. Also one of the points that I like to stress is the fact that conception and pregnancy are physical affairs. Our women are becoming highly cultured. Wherever the civilization curve rises, conception decreases; and if they expect to be pregnant they are going to have to act and live a little more like an animal than they are living at the present time, whether they like it or not.

We also insist upon doing our own examinations. Too many husbands have gonorrhea and also have friends who are doctors. I find in my own private practice that it runs fifty-fifty, that about 50 per cent of the causes of sterility are on the side of the men and 50 per cent are on the side of the women. Dr. Burns seemed to think about 25 per cent were on the side of the men.

Another point that we like to bring out is diet. Too many of our women are living on a lot of sour salads, no breakfast, very little lunch, and a big, gorging dinner, and their diets are very poor in nitrogen. They need more meat, fish, eggs and cheese.

Another thing that has not been mentioned very much here, too, is artificial insemination. You read about it in the newspapers, but you can tell your patients that it will have practically no success and is a very dangerous procedure. I have tried it sixteen times on fourteen different patients only because they insisted that it be done, and none of them conceived. I know of several cases of very severe pelvic infection following artificial insemination.

Another thing to remember, too, is that if you have a patient whom you have been treating and you think that you have had something to do with conception, you should not let your treatment drop the minute she has conceived. One had better keep on with the treatment through the pregnancy, or at least the first four months, because one evidently is dealing with a germ plasm that is faulty and one had better give it all the props he can.

The average physician should be ready to discuss with his sterility patient the subject of adoption. Personally I advise them that if they do adopt a child, it is very wise to adopt a 5-year-old child rather than a baby, because with a 5-year-old one knows what his reactions to his surroundings are, and the woman makes up the time that she has lost in trying to get pregnant. I also do not care to have any social worker pick up a bastard about whom I know nothing and put it in the home of one of my patients and tell her that the baby is so cute it certainly will make a wonderful member of the family. When one adopts a baby one is adopting a future adult. I am quite convinced that most of these high school kids who become pregnant are mentally below par; and I dislike to see a patient of mine accept a baby that already has a couple of strikes against it. I think adoption is one thing that we should be ready to discuss with our patients, to let them know its various angles.

Dr. Robert B. Greenblatt, Augusta, Ga.—Much has recently been said and written about the newer gonadotropic hormones in the treatment of sterility. I should like to stress the fact that the division between the gonadotropic hormones, namely, the urinary gonadotropic-like hormones, the extracts of the anterior pituitary and pregnant mare's serum, is only a relative one. If the dosages were equalized, it may be that the changes wrought in the ovary by them would not be wholly dissimilar.

The impotence of urinary gonadotropic-like hormones in the dosages heretofore used is generally recognized by competent investigators. They cannot be compared to the powerful gonadotropic hormones which are derived from the anterior pituitary, such as Armour's "gonadotropic factor" or Winthrop's "A. P. E.," or those obtained from pregnant mare's serum as "gonadin" (Cutter), "gonadogen" (Upjohn), "anteron" (Schering). Furthermore, the use of these ovarian stimulants in sterility needs much more study and elucidation. Further interpretation is needed to ascertain whether the changes brought about in the ovary are actually progressive or regressive.

I have slides to demonstrate the effect of several commercial preparations upon the human ovary. A follicular cyst with luteinization taking place in the cells of the theca interna was seen after 1,400 Cole-Saunders units of "gonadin" (Cutter) were administered early in the cycle. The theca cells were hypertrophic and their cytoplasm vacuolated. There was no proof that ovulation had taken place. In fact, this luteinized follicular cyst lay in the depth of the ovary and certainly if the ovum were stimulated it must have died, because it had no place to escape.

Changes identical with the above followed administration of 10 c. c. of Armour's "gonadotropic factor" early in the cycle. Abundant sudan-stained lipoids were seen in the cells of the theca interna about the margin of the follicular cyst. Again, evidence of ovulation was lacking. The only thing that could really be said was that ovarian stimulation did take place, as manifested by luteinization of the cells of the theca interna.

The production of ovulation is indeed an important problem in sterility. Great care should be exercised in the interpretation of results. The newer gonadotropic hormones may prove invaluable. Davis and Koff have a beautiful colored illustration in their recently published article of an ovary with two corpora lutea following "gonadogen" therapy. Laparotomy was performed on the seventeenth day of a 23-day cycle. The inference may be correct. However, such a finding must not necessarily be attributed to hormonal stimulation, since it did occur in the later half of the cycle. If ovulation does result from such stimulation, we must demand the evidence: produce the ovum.

An apparently healthy ovum was caught by us several minutes prior to being washed out from an early ruptured follicle. Laparotomy was performed on the tenth day in this patient, with a normal cycle, who had received pregnant mare's serum ("gonadin"). This therapy merely precipitated the ovulation that was going to occur. That pregnant mare's serum may profoundly influence the human ovary is further evidenced by the tag of ovarian tissue that has undergone decidua like change, a phenomenon not infrequently seen in pregnancy.

Dr. M. Y. Dabney, Birmingham, Ala.—This has been as complete a symposium as I have ever heard on the subject. We should praise Dr. Johnson for his wisdom in selecting to present it, a group, rather than individuals scattered throughout our territory. In that way we have very few gaps and very little duplication of data.

I was glad that Dr. Galloway brought up the question of artificial insemination. I do not go quite so far as he does in condemning it and saying that it should not be done. I believe that the indications are few but definite. One of the most important points to remember is that we have too slavishly followed the literature in indications for artificial insemination. Many of the criteria are false and some have been omitted.

Some of the criteria laid down are these: there must be a definite patency all the way from the external os up through the fimbriated end of the tube, and there must be a highly fertile male, with numerous, very active sperms. If that were the case there would be little indication for artificial insemination, because in those cases there is very little left to produce sterility, except endocrine deficiency of either partner.

An indication I have never seen mentioned, but which in my experience has proven important, is the very sub-fertile male, that is, the male who has, say 10 or 15 sperms to the high power field, very sluggishly moving sperms, consistently over several examinations. We know that nature is wasteful, that there are enough sperms emitted at one ejaculation to populate China if every sperm were successful. We know that there is a great waste of them, that relatively few are able to pass the hazards and reach the fallopian tubes. I should like to make this plain, that those subfertile males are the very ones that are the most in need of help. We think of the woman's needing help, but such male sperms need something to help them reach the fallopian tubes.

Dr. Seibel's spoke of two pelvic infections following artificial insemination. The wonder to me is that every case of artificial insemination as now handled is not infected. In the past we have used very poor judgment in the methods of artificial insemination. We still see gynecologists, men who speak with authority, who will have the couple copulate, come to the office and aspirate some of the semen from the vaginal vault and inject it into the uterus, a procedure shocking to one's aseptic sense.

Some years ago I tried to find some means of sterilizing the vagina and collecting a relatively sterile specimen of semen; and this is the technic I have employed: the woman takes about a two-gallon douche of boiled water. The male should have refrained from copulation for a week or ten days to be at his maximum fertility. The vagina is then dried with pledgets and swabbed out with ether very liberally. If the vagina is well dried, ether is a good antiseptic. Ether in the presence of moisture is not to be relied upon. Dry sterile cotton pledgets are used to remove the ether. Then with a blower, remove all further traces of the ether. The next step is to strip the cervix from its under side with a sponge stick carrying a pledget. The cervical canal is aspirated with a glass syringe. The injection, of course, needs no particular description, except to say that one does not need a quantity of seminal fluid, but only two or three drops; and I like to inject it high.

The attempt to collect sterile material from the male is still more difficult, but these points are valuable: I do not think that we should even mention the condom as a method of collecting sperms. The best technic that I know is to have the male wash the penis thoroughly, not once but several times, preferably under a shower, soap the penis several times thoroughly, first voiding, and then wash it clean. A sterile rubber glove, or two sterile gloves, are slipped upon the man's hands after he has washed them, and he should be put in a room by himself, with assurances that he is not going to be disturbed or hurried. He should masturbate, taking care not to touch the end of the penis any more than is necessary, and collecting the specimen in a widemouth sterile bottle. The specimen will then be relatively sterile. Of course, no antiseptics can be used upon the penis.

I have heard only casual reference today to the injection of opaque oils. In my opinion it is a far better method of opening the tubes than with gases. That the Rubin test is an excellent procedure in maintaining tubal patency after it has been proven goes without saying. But oil will create a larger opening if there are adhesions. Viscous skiodan is more bulky and this produces a larger opening. If you inject air or gas it will go through a very small space, and less has been accomplished.

Another useful point is this. When films have been made after oil injections and a "spill" is in doubt, instead of having the patient return the next day for an additional film to determine patency, the patient is moved down to the end of the x-ray table, she is helped into a sitting posture with her feet upon a stool, and is requested to do a "churning" exercise, i. e., she pushes her abdominal wall outward and inward rapidly four or five times to allow the oil to gravitate to the *cul-de-sac*. In that way it is very easy to make the diagnosis of patency at once, a useful course in out of-town patients.

Reference has been made to the use of the stem pessary in some cases as an aid to fertility. I agree with the majority of gynecologists who condemn it on the ground that it acts as a drain in the uterine cavity which it connects with the vagina, one of the dirtiest cavities in the body. I have seen stubborn leukorrhea initiated by this practice and in some instances pelvic infections. Where pregnancy has followed its use, I rather suspect that the preliminary dilatation of a stenotic cervix produced the good result.

Dr. Collins (*closing*).—I cannot agree with Dr. Turner, of Atlanta, that stricture of the cervix does not play a part in sterility. Two years ago Dr. Miller and I reported 47 cases of traumatic stricture of the cervix that followed conization, cauterization and other work on the cervix. Last year Dr. Miller and Dr. Thomas increased that series to 100.

Dr. Turner made the point that if in stricture of the cervix blood can get through, sperm can do so. In 40 per cent of our series of strictures, the women not only had bleeding, but they complained of menorrhagia with the stricture. Whether sperms can get through or not is not all-important. The factors in these strictures are that we find pus, infections and secretions, which in themselves are detrimental to the viability and passage of sperms.

I agree with Dr. Galloway. I, personally, have never performed artificial insemination.

In our definition of sterility, we used the broad term, in which sterility is defined as the inability of a woman to produce a viable fetus. In the strict sense, it is inability of a woman to conceive. I rather like the broad sense, and I heartily agree with Dr. Galloway that once conception has been established, we should treat the woman, even with shotgun therapy, consisting of thyroid extract, the corpus luteum (progestin), and large doses of vitamin E.

As regards Dr. Dabney's statements about iodized oil, I believe he misunderstood me. I said, "if insufflation results are inconclusive," then we use iodized oil or skiodan.

Dr. Thomas (*closing*).—Despite the inadequacy of our present day endocrine treatment, the influence of endocrine disturbances upon sexual function is of great importance and will attain increasing significance in years to come.

Dr. Turner said that retrodisplacement of the uterus plays no part in the causation of sterility. He reasons that in such circumstances the cervix is pointing toward the vaginal orifice and is most favorably situated for direct insemination into this organ. Retrodisplacement of the uterus is considered a very minor and a rather uncommon cause of sterility by most gynecologists, but in occasional instances the correction, by a pessary, of this malposition will definitely relieve sterility. While it is undeniably true that the cervix points forward toward the vaginal orifice when the uterus is retrodisplaced, and seemingly is favorably located for the occurrence of direct insemination, actually the cervix is in the most unfavorable position for spermatozoa, either directly or indirectly, to gain entrance into the cervical canal. In retrodisplacement, the cervix is brought forward close to the symphysis pubis and the penis slips to the side of it and goes back into the vault of the vagina, and direct insemination is practically impossible. Furthermore, the semen deposited in the vaginal fornices, or in the vaginal "pool," is not in contact with the cervix when the uterus is retrodisplaced, and consequently, the possibility of indirect insemination's occurring is very remote.

Dr. Hamblen has referred to the fact that he has never seen any improvement following the use of hormonal therapy in the treatment of individuals with low sperm count or with azoospermia. I can agree with him in that experience. I included this method of therapy in the male because of the fact that Ruben tein has attempted to show that by injection of follicle stimulating hormones, or by injection of pituitary-like hormones from pregnancy urine, he has increased the sperm count in normal individuals. It is a known fact that the sperm count in any individual varies with the degree of what might be termed "sexual exhaustion." After intercourse has occurred several times, the sperms may be very few in number, or may even be entirely absent. Provided sufficient rest is obtained within the next five or six days, the sperm count will increase rapidly. For this reason, it is hard to evaluate any results that Rubenstein has accomplished unless an accurate sexual history can be obtained from the subjects of his experimentation. It has been my own experience, in two cases, that there has been no improvement when such therapy was used in an attempt to evoke spermatogenesis in a male who exhibited azoospermia and in a second individual whose sperm count was extremely low.

There is one factor, not previously discussed, which definitely influences fertility and which should be men-

tioned at this point. I refer to the role played by the vitamins in the occurrence of conception. In the experimental animal, it has been shown that vitamin deficiencies have little, if any, influence upon ovulation, fertilization of the egg, and implantation of the ovum. However, it has been definitely demonstrated that vitamin deficiencies do predispose to the loss of pregnancy. It is our present belief that vitamins A and E, in the female, play no part in the occurrence of conception, but are extremely influential in the maintenance of conception. However, in the male, definite deficiency in spermatogenesis is found to be associated with vitamin A deficiency and vitamin E deficiency. Normal spermatogenesis seems to require the presence of these two substances in the diet in adequate amounts. It is important, therefore, that these substances be administered to the male who exhibits deficiencies in the sperm count provided no organic lesion can be demonstrated to account for this abnormality. Once conception has occurred, it is important that these substances be administered to the female in order that pregnancy may continue.

Insofar as the production of ovulation by the administration of pregnant mare's serum is concerned, it may be stated that in every instance in which this result has apparently been obtained the ovaries have been normal. It may apparently be a very simple matter to produce ovulation in a normal woman by such therapy, but the production of ovulation in a woman who exhibits evidences of an endocrine imbalance is an entirely different matter. Davis and Koff published an article in the *American Journal of Obstetrics and Gynecology* several months ago in which it was claimed that ovulation could be produced in just this manner. The diagram which accompanied the article listed the dates of the injections, the condition of the endometrium as shown by previous biopsy, and the condition of the endometrium as shown by biopsy following treatment. In all of the cases in which the endometrium had presented a condition of hyperplasia, no effect followed the injections of pregnancy mare's serum.

Pregnancy mare's serum cannot be said, in the light of our present knowledge, to have any effect upon an ovary which is showing evidences of abnormal ovarian activity. This substance is definitely active upon the normal ovary and upon the ovary which exhibits a diminished, although not an abnormal, function. Hence, although it may be a fairly simple matter to stimulate an ovary in a normal individual, stimulation of the ovary in an individual who is not normal, and in whom there is definite evidence of either an ovarian or a pituitary disturbance, is quite another problem. No one has ever yet demonstrated the occurrence of ovulation, from endocrine therapy, in a woman who presented evidences of abnormality in that regard.

The viewpoint, expressed by Dr. Hamblen, that these ovaries themselves are refractory, is a very good one and it is one that has been suggested before in the literature. However, it is one that is, so far as our present state of knowledge is concerned, incapable of proof. It certainly seems a very likely possibility.

If we are to produce ovulation in the female, whether in a normal or in an abnormal subject, it seems that much more likelihood of success would follow our efforts if we should make them conform to attempts which have been successful in the monkey. Ovulation in the monkey has been produced by several investigators through the use of a follicle stimulating hormone and either a luteinizing hormone, or a pregnancy urine hormone. Neither a luteinizing hormone nor a pregnancy urine hormone is effective unless the follicle has first been stimulated by a follicle stimulating hormone. Once the follicle has been stimulated properly, by follicle stimulating hormones, ovulation can be produced by the injection, either intravenously or subcutaneously, of a luteinizing hormone or of a pregnancy urine hormone. Accordingly, any attempt to produce ovulation in the human subject should first be preceded by definite stimulation of the follicle with either one of the prepituitary preparations or else with pregnant mare's serum. On the appropriate date, the follicle stimulating agent can be injected intravenously, if the physician is extremely bold, or preferably, the substance can be injected subcutaneously in a tremendous dose. Such injections should be followed, as Dr. Hamblen has mentioned, by injections of the anterior pituitary-like hormone which does possess a fairly definite action upon the corpus luteum once the follicles have been stimulated and ovulation has been produced.

ETIOLOGY AND TREATMENT OF TRAUMATIC SURGICAL SHOCK*

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The term, shock, is used to cover such a variety of conditions that before discussing etiology and treatment it is wise to define the problem accurately. This presentation will deal chiefly with shock caused by trauma to large masses of tissue and that associated with external hemorrhage. It has been shown that a patient may suffer the effects of hemorrhage due to a decrease in the circulating blood volume even though there is no external loss of blood, but only a loss of blood or plasma into the damaged tissues at or near the site of trauma.

Let us consider briefly the reported causes of traumatic surgical shock. Among the many theories advanced as the cause of this condition are the following:

(1) Vasomotor exhaustion.
(2) Fat embolism.
(3) Adrenal theories:
    Hypersecretion
    Hyposecretion.
(4) Respiratory disturbances.
(5) Toxemia.
(6) Local loss of fluids.

While all of these various factors may play

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an occasional or contributory role in the condition, in recent years most attention has been centered on theories 5 and 6, namely, the question of a possible toxic factor formed in damaged tissues, and on local fluid loss into the injured tissues of the animal. Cannon and Bayliss[1 2] (World War Shock Commission), championed the toxemia theory, these authors believing that a histamine-like substance formed in the tissues was responsible for the fall in blood pressure and associated findings. This conception was reached chiefly by experiments which tended to exclude other causes, but never definitely gave positive proof of the presence of such a toxin. Later Blalock[3] and associates and Phemister[4 5] and co-workers performed experiments which demonstrated that the local loss of fluids into the damaged tissues was most often the cause of this type of shock.

Various experiments were performed to prove this. Extremities of anesthetized animals were traumatized until a state of shock existed. The edema fluid of the injured extremity was found to consist of blood and plasma. It was further shown that the quantity of blood and plasma lost from the circulation into the tissues was sufficient to produce profound shock. Since these initial experiments the problem has been attacked from many other angles.

The depletion of the circulating blood volume was further shown by determining the bleeding volume of animals with a low blood pressure produced by a variety of methods.[5] When a carotid artery cannula of a normal dog is opened, about 58 per cent of the calculated blood volume of the animal will be obtained. An animal with a low blood pressure resulting from histamine administration and the associated capillary dilatation will bleed about 50 per cent of its calculated blood volume. In marked contrast to these findings is the fact that the bleeding volume of animals with low blood pressures resulting from severe extremity trauma and from external hemorrhage is only 24 per cent. This shows that in these conditions there is definitely less fluid within the lumen of the vessels.

Roome and Wilson[6] made an extract of traumatized muscle and administered it to a second animal. These investigations failed to demonstrate the presence of a potent toxin in the injured tissues.

During the first World War hundreds of cases of traumatic shock were observed from massive wounds. One group of these cases will be considered briefly, because the principles involved have a practical interest to the surgeon in civil life. Some soldiers on the battlefield were found with severe lower extremity injuries which required the immediate application of a tourniquet. Due to unavoidable circumstances, the tourniquets in some cases were left on for a period of several hours. In some instances it was observed that although when the tourniquet was removed the patient was in fairly good condition, subsequent to the release of the constrictor a state of profound shock gradually developed. This occurred in individuals even though there was no external loss of blood after release of the constrictor. It was observed that a marked swelling of the extremity developed simultaneously with the fall in blood pressure.

Much speculation resulted concerning the cause of the shock following the release of the tourniquet which had been left on several hours. Two Italian surgeons, Fogliani[7] and Paolucci,[8] reproduced the condition experimentally in cats. They believed that toxins were formed in the injured extremities, which, when released into the general circulation, produced the shock.

Wilson and Roome[9] studied the blood pressure curve of both patients and animals following tourniquet use. In patients where the constrictor was left in place for over an hour there was often a temporary decline in pressure; however, this was soon followed by recovery. In the experimental animals the time of constriction was greatly prolonged to compare with the intervals of tourniquet application in the soldiers mentioned above. In these cases prolonged constriction and release (over three hours) was followed by marked swelling of the extremity and a profound and usually fatal fall in the blood pressure. Analysis of the edema fluid of the swollen extremity showed it to consist largely of blood plasma. The amount of fluid lost into the tissues was determined by comparing the weights of symmetrical extremities and was shown to be sufficient to explain the fall in blood pressure and other findings of shock.

Under ordinary circumstances one more commonly fears the complication of temporary nerve palsy from the use of a constrictor. However, it is well to remember this second complication of shock which may develop if a constrictor is left on for several hours.

TREATMENT

Since in this type of shock the circulating blood volume has been diminished, obviously the best treatment is to replace the loss. Im-

mediate transfusion with an adequate quantity of compatible blood is without question the best form of therapy for traumatic shock. Intravenous saline or glucose may be used as only temporary measures to boost the pressure while the patient is being typed. Saline and glucose alone remain in the vessels only a short time and there is evidence to show that when not followed by blood these agents may even tend to wash more proteins out into the damaged tissues. Vasoconstrictor drugs are also of only temporary value. When blood is lost from the circulation, whether it be into the tissues or externally, there is a vasoconstrictor response which helps the body to compensate for the decreased blood volume. The vasoconstrictor drugs simply exaggerate this normal response, but do not correct the essential deficiency of blood loss.

Blood serum is suitable for the treatment of this condition, but is seldom available in suitable quantities.

Acacia has been used with reported success. However, there are also reports of death following its use, a clogging of the reticulo-endothelial system being blamed for the fatal outcome.

It is especially important that replacement of the lost circulating fluid be begun early. It has been shown that if the pressure is left at a critical level for many hours, irreversible reactions may occur which are apt to prevent recovery regardless of therapy.

The modern blood bank has an important place in the treatment of surgical shock in my opinion. It is generally agreed that the administration of adequate amounts of fresh compatible blood is the best form of therapy. However, in a large charity hospital with an active emergency service, this type of blood is not always available. In such circumstances a blood bank adequately managed may save many lives. This has been the impression gained from the observation of cases at the John Gaston Hospital in Memphis. A blood bank is best suited to a large institution where transfusions are frequently needed. Expert supervision of the bank is an absolute necessity.

When a patient is admitted to the John Gaston Hospital who may require a transfusion, 500 c. c. of blood is drawn from the available donors and sent to the bank room. The blood is then typed, cultured, and tested serologically. Before use a direct cross match is made with the recipient. Blood is never kept longer than ten days, since reactions become more frequent after this period of time. Since this bank has been in operation, the number of transfusions given has increased and the percentage of reactions following transfusion has been declining. This is credited to a better standardization of methods.

A large voluntary donor system similar to that in London would undoubtedly save many lives, but as yet such a system has been developed relatively little in this country.

The importance of certain other well known methods in the prevention and treatment of shock should not be overlooked. These include a careful maintenance of the body temperature, rigid hemostasis and the gentlest handling of tissues. The Army slogan of "Splint them where they lie" decreases the shock produced by moving patients with fractures. Local and gas oxygen anesthesia are definitely to be preferred to ether or spinal for the patient in shock.

SUMMARY AND CONCLUSIONS

(1) The chief etiological factor in traumatic surgical shock is a decrease in circulating blood volume.

(2) This reduction in blood volume may result from external hemorrhage or from blood or plasma passing through damaged capillaries out into the traumatized tissues.

(3) The immediate replacement of the lost blood is the most rational treatment whether the fluid has been lost externally or into the tissues of the individual.

(4) The practical advantages of a blood bank for a large charity hospital are emphasized.

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SOME PHASES OF EYE INJURIES: THEIR MANAGEMENT AND MEDICO-LEGAL ASPECTS*

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The management of industrial eye injuries involves much more than the simple repair of local damage to the eye. Today, most of the large industrial plants employ full-time safety directors whose duties are largely educational. The match stem and toothpick artists have been replaced by first aid stations, the personnel of which includes graduates of nursing training schools and college trained men. Executives demand and receive the strictest cooperation between the injured employee and medical attendants. These observations shall be drawn from over 8,000 cases of industrial eye injuries.

The industrial accident eye patient's problem is similar to that of other industrial accident cases in that he is sent to a physician, in the selection of whom he has no part. Furthermore, the physician's fee is paid by the insurance carrier. There are several factors then to be considered, to wit: the patient, his employer, the physician, and the insurance carrier. There must be sympathetic understanding between the patient and his employer with the physician holding the key to the situation. Too often the patient is antagonistic to the medical attendant on first visit for the reason that he is sent. Having scant knowledge of the economic problems involved, the average patient assumes that his industrial accident or insurance physician must be a mediocre if not an inferior doctor or the insurance carrier would not have employed him. The average fifteen to twenty-five dollar per week employee assumes that these big rich insurance companies could not afford to hire a skillful physician. In order to overcome these and other psychological disturbances it is incumbent upon the industrial ophthalmologist to give to these accident cases more than ordinary attention.

When an allegedly injured man enters our office we are usually notified in advance and our office assistant should be prepared to meet the emergency. No private patient would object to our being interrupted for a minute while we give such relief first aid measures. The patient and his attendant should be addressed by name when we introduce ourselves. The local instillation of a drop or two of an anesthetic by the physician himself will do wonders to make him en rapport with his patient. Failure to do this, an air of indifference entailed by some delay, the off-hand direction to an office assistant in the hearing of the patient will require hours or days to rectify, if indeed we can succeed in getting the patient's cooperation at all.

Strictest routine procedures in the course of eye examinations are paramount. There is no place where this is quite so important as in handling the industrial eye case. One should adhere to his routine, slavishly remembering that every such case requires extraordinary care and is a potential law suit. One's routine examination need not be too elaborate to be thorough. I make it a strict rule to take the patient's vision on admission or as soon thereafter as practicable and also on discharge, the dates occupying a prominent part of such record. A full history of the accident in the patient's own words and whether or not any other lay attendant or physician has treated him previously should be obtained. The time of the alleged accident and time of first aid treatment are important. Whether or not the eye under question had been previously normal or injured at any time during the patient's life should be noted and any other vital information should be recorded as soon as practicable. X-ray studies should be insisted upon in all eye injuries where there is a suggestive history or any doubt exists of the presence of an intra-ocular foreign body. Any ophthalmologist who is too busy or unwilling to take these precautions and handle the eye accident after a set routine should refuse such cases and refer them to one who can.

We all know that the eye may become injured in many ways and so delicate are the ocular structures that most of the general men are content to refer their eye injuries to the ophthalmologist at once. The general practitioner views the province of the oculist with such deference that his field suffers few encroachments except by the non-medical refractionist. If we limit our discussion here to those injuries acting upon the eyeball as a whole, we find the greatest number resulting from accidents by workers in the mechanical trades. The frequency of ocular injuries is much higher in industrial than in agricultural districts. The common objects causing severe ocular damage

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include sharp-pointed scissors, knives, explosives, nails, glass splinters, stone or wood chips, iron, steel or brass filings. The latter are in common use in the metal industries. By reason of its exposed position, these flying particles generally strike the eye in the zone of the palpebral fissure or after having perforated the lids. The commonest point of impact is usually in the anterior segment of the eyeball. A perforating injury (generally damaging the cornea or sclera) extends through the entire thickness of the wall of the eyeball. The nature and size of the object, the depth of penetration and the point of impingement are factors of greatest importance. Naturally, the danger involved in non-perforating injuries is much less than in those causing perforation. In injuries of a non-perforating character, the chief danger is that of infection carried by the foreign body or micro-organisms present in the conjunctival sac at the time of injury. When the cornea or conjunctiva is abraded, nature's first line of defense is destroyed and such an eye should have careful first aid. In any such case, a protective bandage should be applied and appropriate antiseptics instilled until the epithelium has regenerated. This usually occurs within 6 to 24 hours in mild cases. When reactions are severe, homatropine or atropine should be used. In young persons healthy eyes suffer little or no ill effect from superficial abrasions on cornea or conjunctiva. Intra-ocular inflammation resulting from such an infection may vary from a mild anterior uveitis to a septic endophthalmitis, depending upon the virulence of the micro-organisms and upon the site of the inoculation. The former may subside within a few weeks and without sequelae of any significance, whereas endophthalmitis leads to atrophy (phthisis bulbi) and blindness. The development of exudate behind the lens makes the diagnosis of endophthalmitis certain. Sometimes the presence of a dense uveal membrane in the pupil prevents examination of the posterior segment of the eyeball. When this occurs, the presence or absence of correct projection of light is the most reliable criterion of the damage in the posterior segment and will aid materially in determining a prognosis and subsequent treatment.

I recently treated a case of violent acute anterior uveitis which required heroic measures to combat. In spite of early atropinization, posterior synechiae formed, together with heavy clumps and fibrinous debris in the aqueous and on the back of the cornea. The synechiae were finally broken by the repeated use of 2 per cent epinephrine barbiturate and 1 per cent solution of atropine subconjunctivally. A stormy and protracted convalescence ensued. The patient suffered severe pain for several days in the early acute stages. Foreign protein shock, large doses of sulfanilamide and local heat were all used, and it was four weeks before the inflammatory process subsided. This condition followed an apparently simple marginal ulcer of the cornea caused by cigar ashes blown into the eye.

These cases should never be regarded as quiet as long as round cells or fibrinous debris can be seen floating in the aqueous, or fibrinous deposits can be seen on the posterior face of the cornea by the slit lamp. Complete atropinization should be continued until all signs of inflammation have disappeared and there is no episcleral congestion.

Aseptic perforating injuries from hot scales occur frequently. Most metal workers are now required to wear goggles and this practice has reduced these injuries to a minimum.

Recently one of my colleagues referred a case in consultation of a healthy young man whose eye had such an injury (LaPat). The patient was working under an automobile and a small brass chip, evidently sterile, perforated the cornea in its upper central portion and lodged in the superficial aspect of the anterior lens cortex. It was centrally located, one could trace its path through the cornea and anterior lens capsule through the undilated pupil in the anterior cortex of the lens. Later he developed a small encapsulating lens opacity, but at no time was there any pain or ocular inflammation. His vision remained good when he was last seen three months after the injury. This was a most striking example of metal tolerance, for at no time was there the slightest inflammatory reaction. One year later, however, an encapsulating central lens opacity developed. The lens and foreign body were removed.

Most victims of this type of injury would not fare so well. Lens damage from perforating injuries of the cornea usually leads to a severe fracture and subluxation of the lens and early cataract. The inflammatory reaction is generally most violent, the media become dense, highly albuminous and secondary congestive glaucoma frequently results, necessitating repeated drainage of the anterior chamber. Such eyes may be saved and a fair amount of vision salvaged if they are treated expectantly. Where the damage is too severe and resulting infection becomes overwhelming, the eye should be eviscerated or enucleated. The choice is largely an academic one and should be left to the judgment of the surgeon. Recurring intra-ocular hemorrhage with glaucoma is always a serious complication.

CILIARY BODY

Trauma to the ciliary body is always a serious matter and requires special care to prevent dis-

astrous complications. It is highly vascular and does not well tolerate traumatism, accidental or otherwise. It is in these cases that our dreaded sympathetic ophthalmias occur. The ciliary body is so sensitive to trauma that mechanical irritation by the dislocated lens may be sufficient to cause increased production of intra-ocular fluid, resulting in secondary glaucoma or worse. The ciliary processes are very delicate structures and may be easily destroyed by mechanical forces. Inflammatory reactions of the ciliary body from direct trauma, without infection, always assume more serious dimensions than those following injury of any other part of the uvea.

Intra-ocular Foreign Bodies.—It is of vital importance in dealing with any perforating injury to decide whether or not a foreign body is retained in the eyeball. In spite of a most carefully taken history, it is sometimes difficult to determine this even after a painstaking examination of the injured eye. The wound of entrance may be traced by a careful examination with loupe and condensing lens. Sometimes the eyeground is obscured by a traumatic cataract or by hemorrhage into the vitreous, in which case even ophthalmoscopic study could not be conclusive. Therefore, if the media are clouded after any penetrating injury, an x-ray examination should be made. Whenever there has been a perforating injury to the eyeball following work on a metal lathe machine and the usual means of examination fail to locate a possible foreign body, a careful x-ray study should be made, and unless it is very small or consists of wood or glass, it can be uncovered and localized and litigation avoided in doubtful cases. Magnetic foreign bodies can usually be removed by the timely application of a strong electro-magnet. Small elliptical chips of steel can best be extracted through a small scleral incision nearest the point of localization. I prefer the posterior scleral route, provided it is embedded in the vitreous or subretinal tissue. If it is in the deep scleral ciliary body or iris or anywhere in the anterior segment of the eyeball, it may be drawn by the magnet into the interior chamber and extracted by magnet or irrigated by means of a keratome incision in the limbus. The best time for a magnet extraction is immediately, or within 24 hours of, the time of the injury. If the foreign body is not removed or is non-removable, the further course of events depends upon its chemical nature, its mode of decomposition, and its location within the eye. Chemically inert bodies such as glass are tolerated best. Metal chips such as iron, brass or copper almost always set up a severe chemical non-bacterial inflammation. The ciliary body is the most refractile tissue in the eye and throws up a large quantity of exudate around the foreign body. This exudate, later on, becomes organized and is transformed into the "bed" of the foreign body. Chips of copper may, by an aseptic suppurative inflammation, force their way out of the eye, usually resulting in a high percentage of visual loss. Iron and copper slowly dissolve in the eye, and the dissolved metal salts impregnate the various ocular tissues, a condition which is called siderosis if the foreign body consists of iron; chalkosis if the foreign body consists of copper. An important consideration develops at this point concerning how much function one is justified in gambling against the dreaded potential loss of the normal eye from sympathetic ophthalmia. We know this may occur months or years later. Provided the function of the eye drops below the amount that can be accounted for by reparable opacities of the optical media, most ophthalmologists will advise enucleation of the injured eye. How long can we afford to temporize? I think the fairest and safest procedure is to inform the patient of the possibility of losing his good eye and let him bear a part of the responsibility of refusal, if in our judgment it is best to enucleate the blind injured eye.

Contusions.—Contusions or non-perforating injuries of the eyeball occur frequently as a result of both direct and indirect trauma. Hard blunt objects striking the eye cause a sudden increase in ocular pressure during the impingement. Immediately following decompression, rupture of the sclera may occur, inflicting a heavy shock upon all the ocular tissue. If the intra-ocular blood vessels are ruptured, a massive hemorrhage occurs into all chambers of the eye. Sometimes one or more ciliary arteries rupture in the suprachoroidal space, and blood is poured out beneath the choroid, pushing the overlying choroid and retina inward and toward the point of the scleral rupture. When such retrochoroidal hemorrhage occurs, arising from a break in the vessel wall during a sudden compression, it pushes a part of the intra-ocular tissues through the scleral opening of the eye and is spoken of as an expulsive hemorrhage. This is one of the tragedies met with in intra-ocular operations and is caused by sudden decompression. It occurs more often in patients with

hypertensive cardiovascular disease, with arteriosclerosis or with ocular hypertension. Hemorrhages often occur from severe contusions following toy torpedo explosions or from the sudden blow from a target shot through an air rifle. When severe, they lead to secondary glaucoma and intractable bleeding from the iris or ciliary body. The treatment in these cases is always puzzling. Complete rest in bed, sedatives and cold or hot compresses are all indicated at different stages. Frequently nothing works. If atropine is used, it tends to embarrass the drainage of the bloody exudate from the eye and emptying the anterior chamber is of doubtful value because one often sees it refill immediately and prolong the hemorrhage. At best, a heavy disciform blood stain on the posterior surface of the cornea results in poor vision and a disfigured eye. These tragedies occur more often in small children allowed to play with firearms.

Scleral.—Scleral rupture follows in the wake of the severest form of blunt injury or contusion of the eye and may be caused by a golf, tennis or baseball, or fist. The thinnest portion of the sclera is the region of the canal of Schlemm, 4 to 4.5 mm. behind the limbus, and it is here that scleral rupture generally occurs. In less severe forms of contusion the cornea is indented and the iris has to carry the pressure of the suddenly displaced aqueous. The root of the iris can recede into the circumlental space, the border of the pupil is pulled away from the antero-posterior axis of the eye, and the pupil itself is suddenly and passively dilated. Iris tears, partial or complete, occur often at the pupillary border. The iris may also be torn at its insertion, leading to a traumatic iridodialysis. Likewise, the sphincter muscle fibers of the iris may be injured, resulting in a permanently dilated pupil without any other ill effect. The zonula fibers are very commonly disturbed and the lens deprived of a part of its suspension apparatus becomes dislocated in the direction of the intact zonula fibers. The most frequent retinal tear occurs at the ora serrata and of the choroid near the disc. This is well illustrated in the traction crescent seen in cases of progressive myopia. The safest procedure would be to remove a dislocated lens. This will avoid frequently resulting uveitis, since the loose lens acts as an intra-ocular foreign body.

Medical and Legal Aspects.—For want of a better guide, we are governed in our estimates of total or permanent loss of vision by the Standard Appraisal table adopted by the House of Delegates of the American Medical Association, Atlantic City, May 25, 1925. This table of percentage loss of visual efficiency is generally recognized by the insurance companies carrying workmen's compensation insurance. Yet this table is sadly defective when we are brought face to face with practical work-a-day facts in many specific cases. A fair and accurate evaluation of percentage of visual deficiency resulting from industrial injuries has to be left to the judgment of the attending oculist. And here is where many of us disagree.

According to the Texas Workmen's Compensation Law, Amended Employer's Liability Act, passed by the 38th Legislature, 1923, compensation is:

> "For total and permanent loss of the sight of one eye 60 per cent of the average weekly wages during one hundred weeks."

A man having an average weekly wage of $25.00 for the previous three working years would receive $1,500.00 in compensation for the total permanent loss of an eye. However, in cases of partial permanent dysfunction, which include 90 per cent of our more serious injuries, the attending oculist should recommend that percentage of loss that will serve as a fair and reasonable basis of settlement. Here is where the policy of our insurance carriers differs quite widely. It is these differences in policy that often lead to litigation and the physician is made to "take the rap" for being unduly biased in favor of the bill payer, namely, the insurance company. Some insurance carriers take our rating, giving the claimant full statutory allowance, but deduct from his compensation the costs of medicines and physicians' fee. In several such cases this would leave the claimant in debt to the insurance carrier if we should strike a trial balance. There is nowhere in our statutes a method of computation for visual field losses or disability from gross cosmetic defect. Pain, lasting photophobia, and resulting errors in refraction are so variable in individual cases that no allowance is ever made or implied in compensating for those injuries. We have all been impressed by the light reflex problem complained of by the patient suffering with corneal opacities. If one of you has ever had a corneal opacity, you will know that glare is a real problem. A large quadrant corneal opacity near the limbus may result in very slight or no loss of central vision, but considerable impairment of function due to the "dazzling" effect

of any bright light. Besides, there is the cosmetic defect which should be evaluated and due allowance made in our permanent partial cases. In other words, a healed sizable corneal opacity covering as much as a limbal quadrant or in the optical center giving 20/30 or 20/40 central visual acuity in many cases should be rated 50 per cent loss in visual efficiency instead of the American Medical Association's 16.4 per cent. Likewise, a small deep-seated central corneal opacity healing from a post-traumatic catarrhal ulcer may result in a corrected visual acuity of 20/25 or 20/30, but would, I think, deserve a much more liberal "permanent partial" rating. Such a central-permanent corneal opacity should be rated 25 per cent if it is important enough to cause dazzling six or eight weeks after the bandage can be left off of such an eye. At the outset, I think all these cases should be given a guarded prognosis. Any permanent corneal opacity, no matter how small, if in the optical center, is more important than one in the periphery or near the limbus.

We do know that nature is very kind in these cases and great improvement will be seen six months to a year later. An eye injury resulting in an unquestioned permanent visual acuity of 20/200 or less should be adjudicated as a vocationally "blind" eye and the patient is entitled to be compensated for "permanent total disability" for the affected eye. In doubtful cases every effort to rule out malingering should be used. And everyone is subconsciously a malingerer when he is suffering from any long-standing impairment of vision due to compensable accident.

Nerve and Oculomotor Injuries.—Cranial injuries resulting in any major sector losses of visual field or peripheral contraction should be given a liberal rating. I think any traumatic injury resulting in paresis of one or more ocular muscles should be regarded as a "permanent total" loss of one eye when persisting without improvement for 90 days or longer. We all know that, barring accident, many of these eyes improve after a year with a surprising amount of functional recovery. These cases should be examined frequently during the interval. A patient with unimproved diplopia following injury is for all practical purposes a one-eyed individual. He is, in my opinion, justly entitled to the compensation of "total permanent disability" of one eye even though both eyes independently may function normally. At best, he will be compelled to wear heavy prisms or have one eye occluded unless he can learn to "suppress." Suppression of the false image in such cases is not always easily acquired and such an individual is limited in his possible vocational followings. I would regard the following eye conditions as of sufficient importance to merit total disability compensation:

(1) Corrected visual efficiency of 20/200 or less due to lesions of cornea, cloudy fluid media of long standing or fundus scarring.

(2) "Tunnel vision," even though central visual acuity may be 20/20.

(3) Intractable diplopia of cranial or ocular muscle palsies requiring use of heavy prisms for its correction.

(4) Hemianopsia, bitemporal or homonymous, if of traumatic origin, in spite of normal visual acuity.

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DISCUSSION (*Abstract*)

Dr. Charles H. Haralson, Tulsa, Okla.—The protective mechanism of the eye is well known and most efficient. The tears inhibit growth of bacteria and the blood supply is ever ready to fill in the breach and conquer any infection that may take place. We have all seen many cases of intra-ocular perforations and lacerations that have gone for hours without treatment, that do not become infected. In fact, it is so unusual to have any infection that one wonders about the wisdom of irrigating the eye with any antiseptic solutions.

Small cuts in the cornea, made by finger nails or cat or dog claws, seem to cause reaction out of all proportion to the injury; such eyes should be promptly dilated, and treated intensively.

Foreign bodies in the cornea rarely give trouble, except when the corneal surface has been traumatized by the use of a cotton applicator or a piece of cloth. Such cases often become infected and cause much concern and disability.

Conjunctival infections, ulcers of the cornea, and inflammations of the anterior segment of the eyeball frequently give a history of a minor injury or exposure to some irritative substance and with or without conscience the patient maintains that the injury is the cause of the lesion. The time to determine the etiology in such cases is when first seen, otherwise much valuable time is lost in treatment, and grave injustice is done anyone who might be held responsible for the real or fancied injury. I have to see my first case of this type that is covered by industrial or accident insurance that does not give a history of injury. It has been my observation that far more money has been paid in such cases than has been underpaid for eye defects not covered by lack of adequate legal evaluation. The ophthalmologist, the patient and the insurance carrier are about equally involved from the standpoint of finance.

Perforating injuries to the lens, producing cataract

and swelling of the lens substance, frequently cause marked increase in the intra-ocular tension, that does not respond to treatment. Such eyes, in my opinion, should have the lens substance removed either with or without iridectomy.

All dislocated lenses should be needled or removed as soon as the eye is free from irritation.

Persistent hemorrhage in the anterior chamber following trauma, usually runs a very protracted and painful course, finally ending in phthisis bulbae. My last two cases were incised and the anterior chamber was irrigated. Both eyes quieted down and made an uneventful recovery.

Traumatic iridodialysis without much apparent intra-ocular damage, in which the eye quiets down in less than three weeks with a clear lens, negative fundus, and good visual acuity, has not been very satisfactory in six cases that I have seen at infrequent intervals over a period of from eight to fifteen years. All of the eyes have lost vision and show degenerative changes. I wonder if excision of the torn iris would not have been the procedure of choice.

My experience with foreign bodies in the posterior segment of the eye is limited to steel and small shot. The latter seem to be tolerated without pain or damage to the eye ball. All steel should be removed as outlined. I always get permission to enucleate the eye in the event that I am unable to remove the metal; one eye out of twenty-eight was enucleated.

I do not believe that a foreign body should be drawn from the vitreous chamber into the anterior chamber with a strong magnet. I lost one eye after such a procedure, and have seen two cases in consultation that were enucleated. The Sweets localization makes the removal of magnetic foreign bodies through a scleral incision a simple surgical procedure, from which there is surprisingly little reaction.

Every physician who treats eye injuries should have to visit the state schools for the blind. One visit will be ample to insure the proper respect for sympathetic ophthalmia. If there is one good eye I think that any questionable eye should be removed.

Penetrating injuries in the region of the ciliary body are always serious and tax the judgment of the surgeon to the utmost; far too many of these injuries terminate in sympathetic disease, and usually the loss of both eyes.

Automobile accidents have increased the number of orbital fractures. Unfortunately they are not often recognized until the swelling has receded and it is too late to save the eye.

Fractures of the base of the skull, intracranial hemorrhage and concussions should be seen by the opthalmologist, who can often give considerable help in the treatment by prescribing rest in bed, dehydration, and withdrawal of the spinal fluid. These measures, when properly used, will do much to minimize the sequelae of head injuries.

All intracranial injuries should be refracted as soon as the patient is ambulatory. Any muscle imbalance should be evaluated and if possible corrected with prisms, along with stimulation of the fusion sense, until the defect is either cured or time has proven that the condition is permanent. In this way many cases of imbalance will make a satisfactory recovery, thereby eliminating a large percentage of those unfortunate cases of suppression and heterophorias that go the rounds seeking relief.

Individuals who have eye disability should be thoroughly informed as to its nature, and the amount of financial recompense that they may justly expect. Similar information to the insurance carrier in the final report usually results in a satisfactory settlement.

Dr. Ralph O. Ryckener, Memphis, Tenn.—It would seem that one should have little difficulty in arriving at a diagnosis of intra-ocular foreign body from the history and clinical findings, if the patient is seen reasonably soon after the initial trauma. However, many times the sensation experienced is no more than that of an ordinary foreign body on the conjunctiva, the symptoms disappear, and a physician is not even consulted until some months later, when the vision fails, or the eye becomes irritable. Even then it is sometimes impossible to obtain a history of trauma until examination discloses signs which point toward the diagnosis of a penetrating injury of the globe. However, I am satisfied that all of us in our specialty need to be more alert in suspecting the presence of intra-ocular foreign bodies in eyes subject to recurrent attacks of iritis, cyclitis, or uveitis.

This conclusion is reached following a review of all the proven cases of intra-ocular foreign body which Dr. E. C. Ellett and I have seen during our fourteen years of association. It was surprising to me to find that of a total of forty-one such cases, eighteen had been seen and treated by at least one physician, some by three or four, without a roentgenogram's having been made or the diagnosis suspected. It was even more astounding to learn that during the latter half of this period statistics grew worse instead of better, for in the past seven years, fourteen of twenty-seven, or more than 50 per cent, fell in the classification described above. That this is no reflection on anyone is evidenced by the admission that we ourselves have been slow to recognize the presence of intra-ocular foreign body in two referred patients in whom the history was inconclusive, and in whom a belated roentgenogram established the diagnosis.

It is possible that we have erred in similar cases of our own, where the patients did not remain in our hands to termination of their symptoms. However, we should make the mistake of too many rather than too few x-ray examinations. The double exposure of an eye on the same plate, with a change in fixation of the globe between the exposures, will yield valuable information at very little expense and save all of us from future embarrassment.

The second point which I wish to stress is the desirability of uniform visual compensation laws for all the states. As industry moves southward, we shall all of us see and treat more cases of ocular trauma, and uniform methods for determining functional visual efficiency would be a distinct aid to all concerned.

For many years a committee from the American Medical Association labored diligently to prepare a schedule of disability ratings based upon losses in visual acuity, visual fields, and disturbances of ocular motility. Their report in 1925 was ratified by the Section of Ophthalmology, and then accepted by the American Medical Association itself.

Of twenty-three states which have adopted some method for computing visual disabilities, eleven have used the basic principles of this committee's report.

As our individual states from time to time in the future prepare legislation to cover this field, we should recommend the incorporation of these principles in the proposed legislation. We may all have our own ideas of the visual efficiency losses suffered by our patients following trauma, but it is unlikely that we can improve in isolated instances on the disability ratings arrived at by the regulations of the American Medical Association schedule; therefore, I feel we should use this method of computing compensation awards until such time as it is replaced by a better one.

Dr. William D. Gill, San Antonio, Tex.—I should like to mention the question of traumatic cataract, a wound to the lens capsule from a foreign body. Do not be sure your patient will develop complete reticular opacity. They do not all develop cataracts that require extraction.

I saw an aviator who tolerated a piece of glass in the lens of one of his eyes for as long as fifteen years, in which no action was apparent as a result of a foreign body, and in another instance I saw that the anterior capsule was perforated with what was supposed to be a thorn, but I doubt that it was a thorn. It was more probably a piece of splinter of some sort. The patient developed only a very minute area of opacity around the point of injury to the lens capsule.

Segmental opacities, where the lens is wounded at its free margin, do not necessarily develop sufficiently to include the entire lens; so when you are advising your patient as to what he may expect from an eye that has been injured anteriorly, in which there is an injury to the lens capsule, you had better be a little guarded because he may retain perfectly good vision in the injured eye.

Now, about extraction of foreign bodies, magnetizing of foreign bodies: I have not been quite so fortunate as some of the men in extracting them through the anterior root. Perhaps my technic is not quite so good, but unless the foreign body is already in the anterior segment of the globe, I have not been able in any instance to drag the body around to the head of the lens and across and get it out through the root; so I have in the posterior type of foreign body used routinely, certainly within recent years, the posterior root for extraction and have been much chagrined to have perfect visual result following extraction, and several months later have the patient come back with a retinal detachment; and I am sure that has happened to many of you.

It makes a difference in rating the patient's disability and a big difference in the way he regards his physician. I have found a little point of technic that may be of value to you. I was advised to try it after I finish magnetic extraction. I do not know whether this is an original idea or not. I have used it for a number of years. After an extraction is completed, simply introduce the actual cautery, cherry red heat, into the wound, and treat as you would retinal detachment. If you leave a cautery there six or eight seconds, you will not have retinal detachments after that.

Each one-tenth of a c. c. of vitreous loss changes the refractive state of an eye one diopter. The eye becomes more plus to the extent of one diopter.

Dr. Griffey (closing).—I trust the time may come when we shall have more comprehensive and uniform laws governing employer's liability in eye injured cases.

HEALTH EDUCATION FOR THE PUBLIC*

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EDUCATE FOR HEALTH AND FOR LIFE

This address is dedicated to those medical men who raise voice to educate the public in matters that offer health, mitigate suffering, and prolong life. Growth and development in the art and science of medicine require that physicians be continuously at study. Is not a similar progress through education, then, a need of the layman? The cause for a high percentage of illness, disability, and death lies in ignorance. Too many are "poor citizens" because they do not understand the fundamentals of health. The medical profession possesses oceans of knowledge pertaining to health, and yet people stand on the seashore and glean little more than pebbles and shells washed in by the tides. The way to a general knowledge of the fundamentals of health should no longer be difficult to navigate, narrow, lonely, and trod by a few. It should be a highway where rapid progress can be made, and open to all.

In June, 1938, it was reported[1] that in the Missouri high schools the basic subject of elementary anatomy and physiology had for some years been made an elective. More than 95 per cent of the graduates of these schools did not elect such courses, therefore had not received instruction in even the most elementary manner in subjects pertaining to structure and function of the human body. During the school year 1937-38, of a total of 963 high schools, only 64 offered courses in physiology.[2] A study at the present time[3] involving 895 high schools upon which complete data are available, exclusive of those in Kansas City and St. Louis, reveals a total of 1,342 students, or only 1.4 per cent of these combined student bodies, enrolled in physiology courses. It is noteworthy that during the last 10-year period the number of course offerings in physiology have decreased, while those in physical education, hygiene, and biology have increased, and through these some instruction dealing with the body and its function is given. Much of the inadequacy of health training in the secondary schools is due to the tend-

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ency of pupils to start specialization too early and to fill their programs with subjects acceptable for college entrance, to the exclusion of fundamental training, even though a comparatively small percentage will ever attend college.

If the above is true of Missouri, what of other states? The State Director of High School Supervision gives assurance that in this matter Missouri is in line with the policies and programs of other states in general, and while it may be a greater offender than some, it is less so than others.[3] No attempt at health education will have far-reaching benefit as long as the pupils in the secondary schools are deprived of the fundamental principles of health instruction, for educators in this field find it almost impossible to impart this information, valuable as it is, to basically uninstructed laymen.

While financial conditions have been responsible for many schools dropping courses which deal with the human body and its functions, it is difficult to believe that economy has resulted, for this involves individual and public health. Life and health have higher and more significant value than anything; in fact, they give value to everything else. They neither offer nor permit substitutions, are ends within themselves, and do not require justification for their conservation. Unfortunately one appreciates their value only when he realizes they are being lost. By every test of a modern business organization, health work, when properly undertaken and adequately financed, pays the best known dividends.

RESPONSIBILITIES

The medical profession should in a manner assume a moral obligation to supply opportunities for the acquisition of health education to those who desire it and be ready to expend thought, time, energy, and patience, if such lay instruction is to yield dividends. The layman who would take advantage of this education must have a sincere desire to learn and profit, and a willingness to cooperate in any projected program.

Like any other human endeavor, health education will be no better than those who undertake it and the interest and enthusiasm put into it. The regard in which the physician is held determines the extent to which he can guide and mold the medical ways of his people. The leadership of the battle against public indifference and general negligence in medical affairs is in our hands. Will we accept, mold, develop, utilize, or leave it for others? In spite of the fact that the national and state medical organizations have taken a positive attitude toward health education, the idea that the doctor must be a teacher as well as a practitioner, is simply not known nor accepted by a large number of physicians.

OPPORTUNITY

Opportunity awaits every unit of organized medicine and is begging for a larger and more comprehensive educational program for the public. Vast resources of medical knowledge have not been carried through to the lives of any people. Medicine today needs to expand beyond the research laboratory, clinic, hospital, and office, into the schoolrooms, homes, and lives of the general citizenship. The research worker and the practitioner must bring their findings and observations within the scope of "the common man's life," who will benefit in proportion to his awareness, knowledge, and use of them. There is scarcely a phase of preventive or curative medical service that does not depend upon education for its effectiveness. Only a rational education over a period of generations can bring the attainments desired.

No one should be guilty of trying to make diagnosticians or practitioners of the lay public, but everyone should become reasonably intelligent about his body and its normal uses and functions. The citizens of America are capable of absorbing enough knowledge of the commonsense type to aid materially in decreasing their illnesses and in delaying deaths. Endeavor must be made to teach the desirability of knowing when medical care is needed and of employing those properly trained. The results of campaigns against cancer and tuberculosis bespeak the possibilities of health education for the public.

PURPOSE

The objective must be for fundamental health knowledge dealing with prevention, wherever practical and possible, and early diagnosis and treatment. There must be an effort to cast out ignorance, fear, and even tolerance of illness, and to replace these with knowledge, hope, and intolerance of ill being. The patient's cooperation and interest in his own welfare is imperative if these are to be accomplished.

The extent of the medical knowledge a people has is a mirrored reflection of the type, char-

acter, and degree of the medical service it enjoys. Who, other than the practicing physician, having contacts with children, parents, educators, and the public in general, is qualified to dispense this knowledge? The doctor of the healing art of medicine should be trained to take such responsibility and to find or create for himself a place in this program. There is no one else competent to advise on premarital matters, guide a pregnant woman over a safe course, deliver the baby, render scientific advice that takes the child through the hazardous years of youth and young adulthood to the age of responsibility, and sees him through his premarital cares and the beginning of a new family. He must be educated to teach and to teach until it does good.

NEED

Public education is one of the most powerful instruments the profession has in its endeavors to dispel fear, prejudice, and hopelessness, to make life less hazardous, disease more amenable to treatment, and to extend the principles of prevention. The avidity with which this knowledge is received by average thinking laymen, especially of school age, is very convincing of their sense of its need.

In addition to educating groups on broad and more general problems, the individual should receive personal instruction as to his particular care and need. A physician should be specific in his advice to the patient. The usual grunt or "don't worry" is not sufficient. Not having adequate instructions, some patients do the most absurd, and not rarely contraindicated things. One must use discretion in what is told the patient, because the doctor may be responsible for the development of certain anxiety states or psychoses merely by telling some things that some patients should not know.

Many cases of diphtheria, typhoid fever, and smallpox are attributable to ignorance, prejudice, or neglect. They have been all but eliminated in communities where immunization is compulsory for school children. Notable decreases are shown in deaths from pneumonia, diphtheria, scarlet fever, typhoid fever, measles, smallpox, whooping cough, and tuberculosis, but many children through carelessness are inadequately protected or even are willfully exposed to some of these diseases in order "to get it over with." Too often deaths from heart disease, appendicitis, and cancer result from procrastination or indifference to one's welfare. Time in some diseases is an all-important factor, and delay in receiving early treatment not rarely results in an economic catastrophe to an entire family.

ACCOMPLISHMENTS

Education has made the public aware that: proof of premarital health should be exacted of those entering into matrimony; consanguinous marriages and marriages with mental or moral defectives are to be avoided; insulin for the diabetic and liver or other extract for the pernicious anemia patient make normal living possible; the administration of sodium chloride to those who lose much salt through perspiration prevents abdominal muscle cramps or myalgia; tuberculosis is largely preventable by eradicating tuberculous milch cows and the isolation of open human cases, and if the disease is acquired it is not a hopeless condition; through an immunization program much childhood illness and many deaths are prevented; when seen early cancer is curable; treatment of eyes of the newborn with one of the silver preparations is a prophylactic measure against blindness; malaria is controllable; vaccination prevents smallpox; the disposal of sewage and control of water supplies have all but eliminated typhoid fever, dysentery, and cholera; the clearing of dairy herds of diseased cattle, cleanliness about the milk house, and the pasteurization of milk have removed the dangers of bovine tuberculosis and undulant fever; and diphtheria is prevented by immunization and cured by antitoxin.

PROBLEM

The public must be made more consciously to realize that the way to sound and beneficial health acquisition, maintenance, and preservation lies through preventive, curative, and corrective surgery and medicine.

The practical problems which lie as a challenge are how to set up effective methods which will afford opportunity for the public to obtain adequate instruction, and having provided it, how to induce its utilization. In this way alone can one fully benefit by the ever-increasing offerings of modern medicine.

Health education ideally begins with the mother who carries it on during the impressionable years in which the child develops. To educate the mothers of today and the future women and mothers of the world intelligently, would

be a certain means of obtaining general aid and public confidence in medicine.

Chevalier Jackson, the inventor of the bronchoscope, one who has rendered conspicuous service to medicine, has been credited with saying that in the fifty years he practiced medicine, at least 85 per cent of his work was devoted to troubles that could have been prevented, and that though he was 72 years old he hoped to have 10 years of more or less active life and wanted to use it to educate people not to need him or others like him. Obviously he believes the really big job is to teach people before they need help, not merely an isolated person here and there, but people *en masse*.

Citizens of America no longer live in dread of cholera, plague, yellow fever, smallpox and a host of other specters. In spite of these achievements there is still a large field to cultivate. The profession holds much little used knowledge and obviously it must be put to gainful work. Too much of the money spent for medical services is for the care of disease and not for its prevention. Practically all universities and colleges now maintain student health services. In nearly all of these the work has been remedial and corrective, with very little effort given to education.

The public press has long wanted and even now pays fancy prices to some authors for articles dealing with medical subjects and services. The public is interested and the newspapers in general should have as a function the education of the people in sound health principles. There is only one source for such information, the profession itself. The material so supplied must, of course, be guardedly authentic and accurate, and preferably should be released by a committee of some organized unit of medicine rather than by an individual.

HOSPITALS

Hospitals at the beginning of the century were little more than boarding houses for the sick. Before that time they were too often looked upon as places in which to die. Today they are institutions affording expert personnel and scientific services to those who occupy free beds, are on reduced rates, or pay the full tariff. They are places where life begins and is maintained, suffering relieved, disease overcome, medically or by surgery removed, deficiency diseases are corrected, and plastic and restorative surgery make livable whole beings from those born with congenital defects or maimed by accidents of industry, modern transportation, or war. The hospitals have gone far in a program of demonstrating to the public the several ways in which they universally render service and aid to health.

LAY OR NONMEDICAL AID

Much of the beneficial education brought forth has been the result of efforts and expenditure of large sums of money by a few corporations, foundations, and interested lay individuals. Under proper guidance they have given to the public factual data and knowledge concerning disease which have enabled the profession to apply more effectively its increasing knowledge. Much research and clinical investigation have been made possible through donations by philanthropic individuals for such purposes or through the creation of endowment funds to maintain investigational work and hospitals. All of this and the proceeds therefrom reflect credit and honor upon those who have made it possible. Medicine has marched forward through such beneficence.

SALES ADVERTISING

Much advertising for the public as it relates to health, no matter under what guise it is conducted, has a potential of doing harm. This particularly applies to the advertising of foods, misbranded merchandise, and patent medicines. No one item of diet is a complete and perfect food, but some advertising would have the credulous believe that this is true. Advertising is especially contrary to the interests of public health when it creates the impression that prepared foodstuffs completely take the place of mother's milk and that certain products, such as vitamins, can replace wholesome, well balanced diets prepared from fresh foods. How can the public understand and properly evaluate the good from the "bunk?" There is need for public education and better control of advertising.

PREVENTION

An important phase of the physician's duty in the prevention of disease is the education of the public. He holds the key position when once he realizes his teaching responsibility to parents, nurses, teachers, school children, industrial workers, and others. Frequently individuals having familial diseases, or who are potential sources for an inherited disease, as hemophilia, certain muscular, nervous and cardiovascular dystrophies, seriously seek advice concerning themselves or the possibility of their marriage.

To whom should they go for such advice? None would say other than the family physician, and the physician of today and tomorrow must be prepared for such responsibility.

THE PROGRAM

A number of plans or trials have been devised, with varying degrees of success, by various national, state, and county societies, clinical groups, medical faculties, and academies of medicine to conduct programs for mass education of the public on health subjects. The daily and weekly press have been employed for the publication of copyrighted articles and for paid advertisements. As an example of the latter, the papers of Johnson County, Arkansas, on June 8, 1939, carried the first of a series in a medical publicity campaign, under the title, "Is Your Doctor an M.D.?" This stressed the importance of distinguishing the doctor of medicine from the faddist and the cultist who usurp the title of doctor.

In so far as I am aware, the California Medical Association has established a precedent. On May 4 of this year that body assessed each of its members the sum of $10.00 for educational purposes and created a "Committee oi Public Education," which was instructed to carry on a state-wide program of education in matters of public health and welfare.[4] Further assessments have been assured if and as the need arises to accomplish the objective sought.

From experience it is believed that great accomplishment will reward any method or effort directed toward adult education that reaches mothers or potential mothers. An educational program under proper guidance can and should be evolved with those entrusted and required by legal and moral obligations to teach and direct youth. Every effort should be made to reach and attempt to teach them when their various programs and health, as well as other, habits are in the formative stage. The adults who unquestionably most need this help are those in the low income groups, the unemployed, and the rural population.

Maternity is a personal experience, but group education has been conducted for and with great benefit to the expectant mother and her coming child through the allocation of Government funds to the various states for this purpose. A similar program could and should be developed to incorporate health training for all individuals receiving Federal, state or local aid, as through unemployment, old age, child welfare, maternal welfare, or relief projects. By this means many could be required to participate or be dropped from relief.

THE SCHOOL AND THE STUDENT BODY

The world is an enormous schoolroom and its entire population a potential student body. An all-inclusive health teaching program should reach the following:

(1) Professional groups, as public health and social welfare workers, school boards or trustees, directors and faculties, physicians, dentists, veterinarians, nurses, and medical students.

(2) Lay organizations of all types and in all walks of life, as the women's auxiliaries to various state and national bodies, church organizations, women's, men's, boys' and girls' clubs, national and state educational associations, including the parent-teacher associations, the legislative bodies of political creation, and schools, including universities and colleges.

(3) Private individuals in conference or in consultation. This is, of necessity, individual instruction involving the professional relationship of physician to patient.

METHODS OF INSTRUCTION

The national, state, county, city and other medical organizations can well afford to proffer the services of speakers to the many lay groups that regularly hold meetings in almost every community. In the schools much can be taught in the general courses of biology, physical education, general science, physiology and home economics. There remains, however, much that cannot be so integrated with other activities and should be taught in one or more courses constructed for the purpose and by those trained for such duties.

Messages or programs may be presented through:

(1) Coordination with nonmedical or medical agencies, in supplying bulletins, pamphlets, posters and placards to be placed in public buildings, schoolrooms, dormitories, street cars, or display windows.

(2) Clinics, as cancer, chest, baby, and diabetic.

(3) The daily and weekly newspapers and popular magazines.

(4) The radio.

(5) The moving picture.

(6) The annual physical examination with advice to govern the patient during the interval.

(7) Conferences between doctor, teacher, and student, or other groups.

(8) Plays, dramatizations, and school events, as May Day parties, health days, and health conservation contests.

(9) Exhibits and speakers at national, state, and county fairs.

(10) Courses in schools, including universities and colleges.

(11) The platform speaker, probably the most effective medium, the appearance in person of the doctor before the lay audience.

Intelligent planning and utilization of the various audiences make possible for this type of education to be conducted in a mass way, in groups, or as personal instruction.

SUMMARY AND CONCLUSIONS

(1) The medical profession is concerned with providing adequate scientific and modern medical service and in protecting the public from the incompetent.

(2) There should be a committee in every medical organization to deal with and further health education to and for the public.

(3) There is need for creation of standards, aims, and ideals for an integrated and coordinated permanent and continuous program on health education. It is obvious that the subject matter cannot be covered in a fixed period of time, and equally obvious that it must be repeated as new groups replace the old.

(4) Timely, trite, accurate, medically supervised health articles should be supplied the daily press.

(5) The most effective health education must be intensive and, to a considerable degree, personal in character.

(6) Courses dealing with personal hygiene, elementary physiology, and health should be required in all grade and high schools. The best education for adult health is the training children receive in schools.

(7) The platform speaker, the physician, the dentist, or a related worker from a health bureau or the nursing staff is most impressive before a lay audience. The physician must be the central figure if he is to regain and hold his place as the interested, authoritative, dynamic, and sympathetic leader in community health.

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MALINGERING RESPONSIBLE FOR LONG-CONTINUED, UNEXPLAINED FEVER*

By SIDNEY SCHNUR, M.D.
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During the past three years, four cases of long-continued, unexplained fever were encountered, each due to fraud. Most discussions of unknown fever in the literature pay scant, if any, attention to this possibility in the differential diagnosis. The recurrence of this diagnosis in the author's experience is evidence to him that malingering, far from being a medical curiosity, is a diagnosis always to be considered and ruled out in cases of prolonged unknown fever.

Certain environmental and clinical findings should arouse one's suspicions. All four patients in this series were females. Two were graduate nurses, while one was an undergraduate. The majority used this means to escape from intolerable environmental conditions. One feigned illness to attract attention and obtain sympathy from her family.

Clinically there was noted a marked disparity between the temperature and pulse curves, the latter being always at a lower level and never paralleling the fever peaks. The white blood count and differential were within normal limits. Because relative bradycardia and leukopenia are not infrequently associated with *bona fide* cases of long-standing fever, these findings will usually not be regarded with suspicion. However, the maintenance of good nutrition and hemic component, and repeated normal sedimentation rates, should immediately raise doubts as to the organic origin of the fever.

The diagnosis is easily confirmed once the possibility is entertained. Several errors must be avoided. (1) Rectal temperature should be taken with the patient lying prone, exposing the buttocks. Oral readings are unsatisfactory because some patients have the ability to raise the mercury level by manipulating the thermom-

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eter bulb with the teeth and gums (Osler). (2) By inserting the thermometer in the rectum himself, the physician prevents "switching" of a fixed thermometer by the nurse or patient. (3) The thermometer should be watched constantly while it remains *in situ*. Fraud is most likely to occur during this stage by the application of the thermometer to hot water bottles, hot plates, or by rubbing on the bed clothes. (4) The thermometer should be removed and read immediately by the physician. One should beware of the trick of "shaking up" a thermometer. This is done by shaking it in the usual manner except that the bulb faces up rather than down.

Two patients produced "fever" by friction with the bed clothes. One applied the thermometer to a hot water bottle which had been given to her for repeated feigned chills. The fourth refused to divulge her method. They were hospitalized three, four, seven, and eight months before malingering was suspected and confirmed. The needless expense involved in subjecting them to the various diagnostic procedures appears in retrospect to be ludicrous if not pathetic. In addition to having most parts of the body x-rayed frequently, all the secretions, excretions and body fluids were examined chemically, bacteriologically and microscopically, and portions of the epidermis histologically. Precipitin, agglutination and skin tests were performed repeatedly.

In summary, malingering should be considered in the differential diagnosis in all cases of unknown fever, particularly in patients who "look too good," and investigation directed early to eliminating this diagnostic possibility.

MYASTHENIA MITIS*

By F. M. Acree, M.D.
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The success of glycine in the treatment of chronic muscular dystrophy and, to an even greater extent, myasthenia gravis, has led to an increasing interest in other clinical uses of this substance.

Glycine is the simplest of the amino acids, and the only one which the human body is known to synthesize. Its synthetic property is proven by the fact that the administration of benzoic acid is followed by an excessive excretion of hippuric acid, a product of the conjugation of benzoic acid and glycine; thus, benzoic acid, which is definitely harmful when free in the body, is neutralized by glycine. This detoxifying power probably accounts, at least in some measure, for the beneficial effect of glycine in certain systemic toxemias. A number of foods contain small amounts of glycine; gelatine, however, is the only food in which it is found in abundance. When the exogenous supply is diminished, the demands of the organisms are supplied, presumably, from stores in the cartilages and fibrous and elastic tissues.

The therapeutic value of glycine lies in its effect upon creatine metabolism. Levene and Kristeller,[12] in 1909, observed a low creatinine and a high creatine excretion in patients with muscular diseases. In 1929, Brand, Harris, Sandberg and Ringer[9] discovered that there was a definite increase of creatine in the urine of patients with progressive muscular dystrophy following the administration of glycine. Milhorat, Techner and Thomas,[15,16] in carrying out further studies on glycine therapy in muscular dystrophy, found that the increase in creatine excretion was followed by a return to normal limits, and that this fall in creatinuria was frequently associated with a rise in excretion of creatinine, the end product of creatine metabolism. Thereafter, studies by these and other investigators, notably Boothby,[6,7] of the uses of glycine were extended to myasthenia gravis and a number of other affections. The prompt rise and subsequent fall of creatinuria upon the administration of the drug was observed, not only in patients with muscular disease, but also in normal individuals in whom creatinuria was not previously present. In contrast to the findings of Milhorat, Techner and Thomas in muscular dystrophy, Adams, Power and Boothby[1,2,3] did not detect an appreciable increase in creatinine excretion in the majority of patients with myasthenia gravis and in a group with miscellaneous diseases; they found that when creatinine was increased, the rise was always slow and gradual. The treatment was far more successful in myasthenia gravis, however, than in muscular dystrophy.

The beneficial effect of glycine is experienced only after its administration over a period of three or more weeks. Clinical improvement becomes apparent coincidently with the fall in creatinuria. Patients develop a better appetite,

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gain in weight, acquire a brighter facial expression and firmer muscle tonus, and become aware of a distinct improvement in their sense of well being, a definite decrease in fatigability, and a greater endurance and impetus to effort. These are common manifestations in the early stages of muscular dystrophy and myasthenia gravis, and in states of fatigue and exhaustion. In fact, not infrequently patients with the milder forms of muscular disease are enabled to resume their normal activities. In the more advanced stages of the myopathies the response is less favorable, though patients are afforded a reasonable degree of comfort. In severe cases, life is often prolonged, periods of amelioration alternating with periods of exacerbation of symptoms.

Glycine appears to be of relatively little value in primary affections of the nervous system, such as progressive spinal muscular atrophy and amyotrophic lateral sclerosis. The fact that creatinuria is not increased following treatment in the majority of these cases would seem to indicate that the lower motor neurone, or trophic unit, must be functionally intact with the muscle for the formation of creatine. This point is regarded as important in the differential diagnosis of neuromuscular diseases and muscular dystrophies. Subjective improvement is experienced by some patients with neuromuscular disease, but is only temporary.

From these findings, it is believed that creatine, even though available, is not utilized or stored. Apparently, therefore, muscle function, which is dependent upon the storage of creatine, is directly affected. Reinhold[20] and his associates, in fact, found a decided improvement in the quality of biopsy specimens of muscle tissue of patients with muscular dystrophy following glycine therapy, as compared to similar tissue removed before treatment. Reese and Burns[19] have explained the physiologic process in the muscles on the theory that the energy for contraction is produced by the breakdown of phosphagen, a compound of creatine and an organic or inorganic phosphate, while the production of lactic acid provides the energy for the resynthesis of phosphagen; if the formation of creatine is dependent upon the storage of glycine, muscular contraction is probably disturbed because of a secondary depletion of creatine and consequently of phosphagen in the muscle. Or, they state that a hypometabolic activity in the dystrophic muscle may be responsible for the disturbed physiologic process, and that this activity may be accelerated by an excessive ingestion of amino acid. Adams, Power and Boothby are of the opinion that glycine itself may be a precursor of creatine, or may merely stimulate or change the course of metabolism in general, causing a definitely increased formation or decreased destruction of creatine, rather than a forcing out of normally pre-existent creatine.

The dosage of glycine must be governed by the nature and extent of the affection. Patients with definite muscular diseases may require 5 gm. three to six times daily, whereas those whose complaint is only a simple chronic exhaustion or fatigue often require only 1 gm. or less three times daily and, in reality, cannot tolerate the larger doses. In the primary myopathies, treatment must be continued indefinitely.

Since the incidence of primary muscular diseases is comparatively small, perhaps the chief interest in this drug lies in its usefulness in the milder asthenic disorders. Complaints of chronic exhaustion and fatigue are heard in every day practice, yet these are little understood syndromes, for which we have heretofore been able to recommend no effective treatment other than rest. McGuire[14] suggests that the term "myasthenia mitis" be applied to these affections, as distinguished from the more serious primary myopathies.

At the Mayo Clinic numerous investigations have been carried out in this field. Boothby,[6,7] Hench[11] and Wilder have been studying the effect of glycine upon the acute muscular fatigue of athletes, and chronic fatigue from overwork, infection, and nutritional deficiency. They have also attempted to evaluate the drug in the treatment of patients with complaints of indeterminate nature, who have little, if any, actual pain, but are always exhausted and sometimes hyperemotional, and whose condition usually is diagnosed as chronic nervous exhaustion, as well as those who experience vague muscular aches and pains associated with mental and physical depression and exhaustion. Some of these patients were partially or wholly relieved. Others, however, were not benefited; this, they believed, may have been explained by the fact that they were not always able to determine to what extent the complaint was of psychogenic or neurogenic, rather than metabolic origin. They found that neurotic, frankly nervous patients were less likely to be improved, whereas those with more stable nervous systems were enabled to go further and do more before becoming fatigued.

These authors suggest that glycine may like-

wise be beneficial in cases of chronic fibrositis or "muscular rheumatism," wherein patients complain of stiffness and soreness of tendons, muscles or joints, and the pathologic changes are supposed to be inflammatory hyperplasia of white fibrous tissue with the formation of subcutaneous nodules or intramuscular fibrous thickening, as distinguished from the symptoms and pathologic changes incident to intra-articular arthritis. They further suggest the trial of glycine as a measure for relieving the generalized muscular weakness and exhaustion accompanying arthritis.

Beard[4,5] and his co-workers observed that the ingestion of amino acid was followed by an increase in weight of normal individuals who had been unable to gain weight by dietary or other measures. Because of its effect on protein metabolism, they also administered glycine to patients who were allergic to different proteins, with successful results. They found that skin lesions associated with allergic conditions disappeared upon the ingestion of glycine, and attributed this to the detoxifying power of the drug.

The author's experience with glycine covers a period of approximately two years. The first case in which it was used was that of a child 3 years of age who became totally paralyzed following a streptococcic infection of the throat. The paralysis involved not only all four extremities, but also the muscles of the eyelids, the neck and throat, and to some extent even the tongue. After six months of treatment with glycine, the paralysis had entirely disappeared, and the child has since been in excellent health.

Six patients with paralysis agitans, all men of advanced years, have received glycine for a period of one to four months. Four of the number have been materially benefited, while two have improved to a noticeable extent. All are still continuing the treatment.

A patient with pernicious anemia of several years' duration had been taking, in addition to liver extract, sodium cacodylate for the relief of an arthritic type of pain. After five or six weeks of glycine, her pain subsided completely, permitting withdrawal of the sodium cacodylate, her general physical condition improved, and she exhibited a much more cheerful mental attitude. Another patient had become profoundly fatigued and depressed during a severe menorrhagia which had been controlled only by radium. A few weeks of treatment with glycine have not only restored her to normal activity but, as in the preceding case, have given her a distinctly brighter mental outlook. It is quite possible that much of the complaint of these two patients was of psychic origin; even so, the beneficial effect of the glycine was without question primarily of a physical nature.

Glycine has been administered to fifteen other patients whose only complaint was an excessive fatigue of both mind and body. A few had been found to have a malarial infection, for which they had received a thorough course of antimalarial therapy, without any effect upon the fatigue. After taking glycine for three to six weeks, the majority of these patients reported a renewed willingness to carry out their duties and a definite increase in physical endurance.

The usual dosage of glycine in the foregoing cases was 6 grams daily in equally divided doses. The patient with pernicious anemia, however, was unable to tolerate more than 1 gram three times daily. Glycine in a wine medium was prescribed for all patients except those who presented a contraindication to this form.

The author feels that the results obtained in these cases justify a more extensive use of glycine as a treatment of myasthenia mitis, mild muscular weakness or excessive fatigue, whether observed alone or in association with definite pathologic disturbances.

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DISCUSSION (*Abstract*)

Dr. Samuel S. Riven, Nashville, Tenn.—This paper is of interest for various reasons: among them, it introduces the term myasthenia mitis, a condition resembling if not related to mild instances of myasthenia gravis, and emphasizes the metabolic disturbances of this disorder. It would be of interest to know whether the cases reported by the author were made worse by the administration of quinine, as true myasthenia gravis always is.

At Vanderbilt we have treated ten cases of myasthenia gravis in the past five years. The symptoms in these patients were of varying degrees of severity from very mild instances to the very severe forms. The series offered an opportunity to make some comparison of the relative efficiency of the various drugs used in the treatment of this disease. The method used included not only symptomatic improvement as related by the patients, but ergographic examinations as objective evidence. I should like to discuss the effects, as shown by ergographic tracings, of the following drugs, namely: glycine, ephedrine, prostigmine and guanidine hydrochloride. We had little success with glycine in ambulatory patients, but when the patients were at rest in the hospital the administration of glycine was associated with some improvement. We have been inclined to attribute the improvement to the rest rather than the glycine; we also believe that some benefits derived from the glycine and other amino acids are due to their specific dynamic action and to the increased caloric value they add to the diet.

We have made ergographic tracings of a patient with myasthenia gravis whose symptoms were rather mild to illustrate the extent of the muscle fatigue and the response obtained after the administration of various drugs.

We feel that prostigmine now has been definitely established as a diagnostic test. If 1 c. c. of prostigmine is given intramuscularly to a normal patient, his muscular effort is improved, and this lasts for a period of two hours, if tracings are made at a half hour, one hour, and two hours. Six hours after the administration of prostigmine intramuscularly the effect is entirely worn off.

In a normal control, after the administration of ephedrine, three-eighths of a grain 3 times a day, fatigability occurs almost immediately. If after ephedrine we again give prostigmine, we observe the contrast in effects.

If after one month of administration of glycine by mouth, 15 grams daily, to a normal control, ergographic tracings are obtained, there is practically no effect. The ergographic tracing resembles the control. Administration of glycine or other amino acids effects the subjective improvement of the patient by the specific dynamic action of the protein or by adding caloric intake to the diet. It is also of interest to note that in none of our patients were we able to demonstrate creatinuria after the administration of glycine. We have been able to demonstrate slight increases of creatine in the urine only in the acute or severe relapses. We also believe that creatinuria appears when there is a great deal of muscular atrophy from disuse.

In 1938 we reported improvement in muscle function after the administration of guanidine hydrochloride. Dr. Minot, working at Vanderbilt University, was able to show an increased irritability in muscle after the administration of guanidine. She also noted that prostigmine had a very short lived effect, that in severe instances of myasthenia gravis the action of prostigmine was brief, and in very severe instances it produced a very serious relapse, a let-down, in muscle function, and in certain instances where the condition became very acute it lost its effect entirely. Because of that, and because of her previous work with guanidine hydrochloride, she suggested and tried the administration of guanidine hydrochloride in one case and found that it improved the condition very rapidly. At this point we entered the problem and treated six instances of myasthenia gravis, from very mild instances to very severe cases, with this drug. From the ergographic response, fatigue occurred very rapidly.

If 6.6 milligrams of guanidine hydrochloride per kilo of body weight was given intravenously within 30 minutes after its administration muscle function improved. This effect lasted eight hours in contrast to the effect on this same patient of prostigmine, which lasted only two hours. We feel that the response to guanidine and the response to prostigmine must be a functional one, a physiologic one, and not a metabolic one, because it is rapid and dramatic.

Guanidine hydrochloride works just as efficiently by mouth. The same dose, 6.6 milligrams given by mouth, will produce a response which lasts 7¼ hours.

Guanidine hydrochloride can be given with other drugs. We have combined it in very severe instances of myasthenia gravis with prostigmine. The effect of prostigmine alone may be noticed, and then the enhancement of the effect by the administration of 250 milligrams of guanidine hydrochloride by mouth, together with prostigmine, in instances where prostigmine alone does not adequately restore muscle function.

We do not claim that this new drug is a cure for myasthenia gravis. It is of physiologic interest because it brings us closer to the understanding of the disorder, the cause of which is unknown.

Dr. Charles H. Lutterloh, Hot Springs, Ark.—The value of glycine in the treatment of myasthenia mitis has been generally based on subjective observations. In addition to the work of Boothby, Hench and Wilder

on the effect of glycine upon the acute muscular fatigue of athletes, this year Ray, Johnson and Taylor have made significant contributions to existing knowledge in this field with their publication of an objective study on the effect of glycine on a group of ten athletes. The fatigue level was determined on this group with the aid of a bicycle ergometer for three periods: (1) a control period without glycine or fruit juice; (2) during period when glycine was administered in a fruit juice suspension; and (3) another period when only the fruit juice was given. The results showed that only when glycine was given was there an increase in the amount of work produced before the fatigue level was reached, this increase varying from 37 to 240 per cent above the training level.

From this experiment and the work referred to by Dr. Acree glycine seems definitely to exert a beneficial effect on the fatigue syndrome. It seems to me that the only criticism which might be offered is not the use of the drug in the conditions mentioned, but the term "myasthenia mitis." Is there any justification for the use of this term in preference to much simpler terms as "fatigue states," "effort syndrome," or "exhaustion states?"

Dr. O. P. J. Falk, St. Louis, Mo.—I want to report my own clinical observations on the use of glycine. I recently reported a group of 50 individuals that I have had under glycine treatment for several months, for what I have termed "nonspecific asthenia."

The favorable effect of glycine on myasthenia gravis and progressive muscle atrophy has led to its use in other less clearly recognized conditions, unassociated with any type of known muscular pathologic change, such as are included under such terms as "pathologic fatigability," "chronic exhaustive states," or "fatigue neurosis." Although many of these cases fall under the general heading of "functional states" or so-called "nervous dispositions," it has been my observation that the most favorable results obtained from this substance in the treatment of the functional states were in those individuals who presented a picture of chronic exhaustion rather than a highly neurotic temperament. Many of these individuals come in the category of what I have termed "constitutional physiopath." They frequently give a history of having felt tired and weak and unable to cope with their situation in life for a period of years. I have been observing the effect of glycine on a group of cases presenting a syndrome characterized by weakness, underweight, ready fatigability, exhaustion, often accompanied by anorexia, and inability to gain weight, altogether presenting a picture that might be best described as a "nonspecific asthenia." Naturally this group of cases has been carefully checked over, and any primary constitutional or infectious state ru'ed out. Differential diagnosis of this rather vaguely defined syndrome is difficult, and must necessarily carefully exclude such conditions as hypo-adrenalism, Simmonds' disease (pituitary cachexia), atypical thyroid states, occult tuberculosis, obscure gastro intestinal and cardiovascular disease, latent syphilis, chronic malaria and undulant fever, as well as certain instances of obscure allergic states that might, by continued annoying symptoms, produce a state of chronic fatigue.

Glycine is the simplest of the amino acids and is the only one that the human body is known to synthesize. It is believed that the cases which are benefited by its administration are those in which the natural production is not sufficient to meet the needs of the body. It has been found that patients with progressive muscular dystrophy and myasthenia gravis can take as much as 30 grams of glycine daily without disagreeable symptoms, but patients with fatigability of less specific types do not tolerate such large doses. Many patients who were formerly considered neurotics or suffering from chronic nervous exhaustion have been found to be markedly benefited by a moderate daily intake of glycine. No laboratory tests have been developed by which we can forecast which cases will probably be benefited. The presence or absence of creatinuria has not proven to be a reliable determining factor, although it has been shown that the administration of glycine does influence the metabolism of creatine.

Any individual who, without apparent cause, feels unduly weak and tired after only moderate exertion is certainly not normal. We should recognize this syndrome and after carefully ruling out any other condition that might be responsible for undue and otherwise unexplainable muscle fatigability, recognize this condition as "nonspecific myasthenia" or "myasthenia mitis," as Stuart McGuire and the essayist have termed it.

The evaluation of therapeutic results from treatment of such a purely subjective disorder is necessarily very difficult, and may be influenced by other factors, known or unknown. We have tried to minimize the factor of suggestion and have attempted to gauge the response to therapy by reports on the change in the patient's ability to perform certain specified activities, as well as an increased feeling of well being, enhancement of muscle firmness, gain in weight, diminution of fatigability, or sense of exhaustion.

I have been observing the effect of glycine on 50 cases over a period of the last eight months: 28 women and 22 men. After applying all the criteria described in ruling out any primary factors which might be concerned in the production of their symptoms, I felt justified in classifying them as "nonspecific asthenias." Each of these cases was given an average of 10 grams of glycine in fruit juice or cereal with the morning meal. Of the 22 men, 15 reported definite improvement in their fatigability, feeling of exhaustion or inaptitude to mental or physical exertion. Of the 28 women, 7 were helped, 6 reported questionable results and 15 reported definite improvement. The syndrome in the women was more frequently characterized by such complaints as weakness, ready fatigability and exhaustion, often accompanied by loss of appetite and sometimes by emotional instability and palpitation. Classifying the questionable cases with those not improved, I feel that half of our female subjects were benefited and half received no apparent benefit from the glycine. Comparing these two equal groups, we found no outstanding differentiation in such objective findings as basal metabolism, blood pressure, age or weight level. The average woman who reported benefit was 47 years of age (ranging from 27 to 66), had a basal metabolism of minus 3 per cent, blood pressure of 108/70 and weighed 122 pounds. The average findings in the woman not benefited by the treatment were: basal metabolism minus 3 per cent, blood pressure of 120/80, age 49, and weight 123 pounds. The only notable difference between the two groups

(and that to a very slight degree) was the moderate difference between the average blood pressure, 108/70 in the group benefited, compared to 120/80 in the group reporting no improvement. This difference in blood pressure was not found in the two groups of our men, two-thirds of whom reported improvement from the treatment. Of the improved group, the average age was 42, weight 152 pounds, blood pressure 115/75, and basal metabolism minus 7 per cent.

TREATMENT OF SCARLET FEVER*

By HARRY J. JACOBSON, M.D.
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The treatment of scarlet fever has greatly advanced since 1923 when Drs. George F. and Gladys Dick[1] reported the successful production of scarlet fever in human beings, by the method of swabbing throats of volunteers with pure cultures of hemolytic streptococci isolated from typical cases of scarlet fever. They further proved that the organism did not act upon the skin to produce the rash, but produced a soluble toxin which in turn was responsible for the rash. This toxin was neutralized by convalescent serum and by the serum of individuals immunized by graduated doses of toxin. Through this work they were able to offer a method of controlling the disease: (1) by identification of scarlet fever streptococci through neutralization of the toxin by specific antitoxin; (2) control of quarantine by culture on blood agar plates; (3) skin tests with toxin which within 24 hours determined susceptibility; (4) by actively immunizing those susceptible to scarlet fever; and (5) by a specific antitoxin useful in the treatment and diagnosis of the disease.

Susceptibility can be ascertained by an intradermal skin test in which 0.1 c. c. of scarlet fever toxin is injected into the flexor surface of the forearm and read between the twentieth and twenty-fourth hour. Unlike the Schick test there is no induration. The slightest blush or erythema denotes susceptibility, the more intense the reaction the greater the susceptibility. Twenty-four thousand individuals with negative Dick tests have passed through one or more epidemics without contracting the disease. Two thousand one hundred and fifty-seven students, nurses and interns with negative skin tests were allowed to go on duty which involved intimate prolonged contact with scarlet fever patients, and none of these contracted the disease.

Those found susceptible to scarlet fever may be immunized by subcutaneous injections of graduated doses of scarlet fever toxin. The doses should be correctly graduated so as to give no harmful reaction yet confer adequate immunity. The Dicks immunized 13,000 persons without injury. In a large series of cases, including high susceptibles, the Dicks report reaction in 10 per cent, Park 10 per cent, and Gordon of Detroit 15 per cent. As a rule, five doses are given, starting with 500 skin doses and increasing to a final dose of 80,000 to 100,000 skin doses given at weekly intervals. Two weeks after the last dose they should be tested for immunity by intradermal injection of 0.1 c. c. toxin in one forearm, 0.2 c. c. in the other. If the reaction of either is positive, repeat the last dose. Ninety-five per cent are immunized and in the remaining 5 per cent, the susceptibility is modified. Retests after six years show 90-95 per cent still Dick negative, while 5-9 per cent must be re-immunized.

Convalescent serum in doses of 10 to 20 c. c. have been suggested in actual contacts to be followed in 10 days to two weeks with active immunization.

Scarlet fever antitoxin in prophylactic doses has not proven satisfactory due to the short incubation period and the severity of the reaction produced.

Since 1923, there has been marked advancement made in the active treatment of scarlet fever. Previous to this, symptomatic treatment only was used. Today we may give scarlet fever antitoxin, convalescent serum or sulfanilamide, or a combination of serum and sulfanilamide.

Sulfanilamide.—Sulfanilamide according to Wesselhoeft and Smith[2] does not affect the rash nor fever of the disease, hence does not exert any appreciable effect on the toxemia. They feel antitoxin should be administered early in the toxic stages of the disease.

In one hundred control cases and one hundred cases treated with sulfanilamide, they found that otitis media and cervical adenitis were less frequent in the treated cases. Otherwise there was no difference. Peters and Havard in England, in 150 cases, found that the complications were reduced from 56 to 35 per cent in the treated cases. Sulfanilamide used in the last week of convalescence has been shown not to reduce the

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carrier rate through eradication of hemolytic streptococcus from the nose and throat.

The use of sulfanilamide as a prophylactic in nonimmune contacts is a problem for carefully controlled investigation. Platou[3] gave 60 intimate contacts sulfanilamide as a prophylactic with no infection in any of these.

One hundred and two cases of scarlet fever were treated with sulfanilamide only, between February, 1937, and August, 1939, at Isolation Hospital, Memphis, Tennessee. There were no deaths. One case with severe toxemia, sepsis and nephritis was given convalescent serum and antitoxin along with sulfanilamide and recovered. In this series of cases which ranged between eight months and thirty-three years of age, dosage was computed as 3/4 to 1 grain per pound of weight per day, one-half the 24-hour dose being given immediately. Sulfanilamide medication was continued in reduced amounts throughout convalescence. Fifty grains of sulfanilamide was the smallest total dosage and 655 grains the largest total dosage. Daily complete blood counts were done. Sulfanilamide concentration estimates were done on every case. Cyanosis without sulfhemoglobinemia was disregarded and treatment continued. A few cases exhibited toxic effects of the drug. One patient developed jaundice on the tenth day, which disappeared upon discontinuance of the drug. Eleven cases developed anemia, which was improved by blood transfusions and cessation of the sulfanilamide. The average period of fever in the uncomplicated cases was 3.9 days. Complications were as follows:

Adenitis	8 cases
Otitis media	6 cases
Nephritis	3 cases
Myocarditis	1 case
Mastoiditis	1 case
Sepsis	1 case
Jaundice	1 case
Sinusitis	1 case

Two cases of postoperative and traumatic scarlet fever responded quickly to the drug.

Convalescent Serum.—Our experience with convalescent serum has been limited, due to the difficulty of obtaining it. In larger centers such as Chicago, Serum Stations with large amounts of pooled serum have been set up making it easily available. It is safe to give and may be used intravenously with safety in critical cases. Dick has suggested using pooled serum of Dick negatives. According to Fox, Hardgrove[4] and others, there is only one per cent reaction with convalescent serum as compared to 35 per cent with antitoxin.

Tap and Young[5], in Detroit, in 346 cases, found convalescent serum and antitoxin equally effective in treatment of moderately severe scarlet fever. The therapeutic dose of convalescent serum is from 30 to 100 c. c., depending on weight.

Scarlet Fever Antitoxin.—The dosage is 6-10 c. c. or 6,000 units given intramuscularly. Patients should be tested for sensitivity before it is given. It has been shown that the earlier it is given after onset the better the results. In the toxic individual with intense rash, disturbed sensorium, rapid pulse and high fever, the therapeutic dose of scarlet fever antitoxin often gives dramatic results. In 12 to 24 hours the fever falls sharply and the patient's general condition is much improved. In private practice we feel that every case of moderate or severe scarlet fever should have antitoxin along with sulfanilamide. Since any mild scarlet may develop severe complications, I feel that this is the better treatment for any case of scarlet fever.

From 1935 to 1937, sixty-seven cases were given antitoxin. In 1938-39 two additional cases were given antitoxin, one in combination with sulfanilamide. These cases were seen one to five days after onset. There were two deaths from sepsis. The dosage was 6,000 units intramuscularly, the ages from 18 months to 36 years. Nineteen, or 27.5 per cent, developed serum sickness. In uncomplicated cases, fever averaged 48 hours. Complications were as follows:

Cervical adenitis	14
Otitis media	7
Sepsis	3
Mastoiditis	1
Peritonsillar abscess	1
Nephritis	1
Sinusitis	1
Cellulitis (neck)	2

Symptomatic Treatment.—Many cases of mild scarlet fever have made uneventful recoveries without the use of sera or sulfanilamide. It is necessary to isolate the patient either in the hospital or in a room if kept at home, from other members of the family. Washing with soap and water on the hands of the examiner and the skin of the patient is the only procedure necessary for sterilization. Mask and gown should be worn by the physician and the attendant. For the care of the skin olive oil or vaseline will suffice. Quarantine time varies in different lo-

calities from 21 to 30 days. Cases with complications such as rhinitis, sinusitis and purulent otitis media are kept in quarantine until they are cured.

Diet.—A liquid diet is used for the first day or so. After that unless the patient has actual nephritis, he is allowed to eat anything he wishes. In case of nephritis with edema, liquids and protein intake may be decreased, and a diet low in proteins and salt substituted. Convulsions due to an acute uremic state are best treated by magnesium sulphate given intravenously or by mouth together with the old-fashioned sweat pack. Restlessness or pain are best treated by opiates or barbiturates. Fever may be controlled by antipyretics. When edema and obstruction of the larynx occur tracheotomy should be done immediately. It is best to keep these patients in bed for at least two weeks to prevent complications. For the nose and throat, antiseptic nasal drops and swabbing with an antiseptic solution can be employed, although Toomey and others consider this a worthless procedure. The ears should be watched carefully and opened at the first sign of trouble. Adenitis should be treated expectantly with avoidance of incision if possible. The radiologist and otologist should be consulted where the ear discharges for more than a month for the obvious possibility of mastoid involvement. Sinusitis should be treated conservatively with heat and postural drainage.

CONCLUSIONS

(1) Many cases of scarlet fever recover spontaneously without specific treatment.

(2) Any mild case of scarlet fever may develop serious complications so that specific medication is always in order.

(3) Active immunization with scarlet fever toxin despite reaction in 10-15 per cent of cases should receive serious consideration. This is especially effective in control of epidemics and in hospitals and institutions exposed to the disease.

(4) A practical scheme of treatment would be a combination of serum and sulfanilamide with necessary symptomatic treatment.

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THE USE OF OXYGEN IN JOINTS IN PREVENTING ADHESIONS FROM TRAUMA AND INFECTION*

By E. Bennette Henson, M.D.
Charleston, West Virginia

In the February, 1930, issue of the *West Virginia Medical Journal,* a preliminary report was made of the use of oxygen under pressure in dry knee joints, to break up adhesions. A further report was made at the St. Louis meeting of the Southern Medical Association in 1935 and published in the June, 1936, issue of the Southern Medical Journal. Mention was made then of the use of oxygen to prevent the formation of adhesions in the acutely inflamed joint and the recently injured joint.

The acute joint will be discussed here and the same method of injection is used as in the dry joint, with this difference: in the dry joint, the oxygen is injected under known pressure (sometimes as high as 12-pound pressure) while in the acute joint a needle is inserted through the capsule and as much fluid as possible is withdrawn. Oxygen is then allowed to flow in to the point of the patient's tolerance, but no effort is made to inflate an already stretched capsule. Since the needle necessary to remove the fluid is rather large, compression at the point of needle puncture should be maintained for several minutes to prevent escape of oxygen from the joint.

All of the larger joints have been treated with oxygen, except the hip joint. No hip case has presented itself that seemed appropriate. Only ten cases with finger joint involvement have been treated. The small joint presents a difficult problem. The patient is reluctant to consent to have a needle puncturing his finger joint. Consent is not difficult to obtain for the other joints. The knee represents the most frequently treated joint, and since the patella makes of this joint a particular problem, especially in injuries of the entire lower extremity, a few observations may be in order.

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

In a rather large series of injuries since the World War, the writer has found that if the patella could be kept free of adhesions, some motion of the joint could be expected. Manipulation under anesthesia was often resorted to in years past. However, in the past five years, no such procedure has been necessary; neither have such means as wedge casts or turn-buckle casts been necessary.

The infected joint has not been seen frequently in the acute stage. Physicians are slower in referring such cases than formerly, but those cases, when seen in the first two weeks of onset, make satisfactory progress.

The aspiration and oxygen injection combined have done two things in the cases coming under observation: first, the patient feels a sense of relief, and secondly, the capsule assumes a more normal appearance, and palpation of the joint is allowed without much fear. Apprehension is greatly lessened. Many times the patient attempts, of his own volition, to move the joint. The time of splinting has been lessened. No case treated has had a flare-up, either at the time of injection or following injection. No so-called dry joint has occurred.

Great care has been used in selecting cases for oxygen treatment. No attempt has been made to create a large series of cases. In truth, cases were passed up that later were regretted. The series is based principally on cases in private practice and not in a charity clinic.

Only two case histories are presented, one of recent trauma, and one of infection. Both cases are of the knee.

A man, 62 years of age, was run down by an automobile, causing a severe fracture into the left knee joint. Twelve hours after the accident, 100 c. c. of bloody fluid was withdrawn and approximately the same amount of oxygen was inserted through the needle, and the needle quickly withdrawn, leaving the oxygen in the joint. Two weeks later, 50 c. c. of fluid was withdrawn from the joint and an equal amount of oxygen was put in; again in two weeks, a third injection, this time only 20 c. c. At the end of eight weeks the range of motion of the knee was 90 degrees without pain or effort. In the meanwhile, the patient had been continuously in a plaster cast.

Another type of case is one of acute infection. A man aged 35 years had a very acutely inflamed and swollen knee, in which 50 c. c. of infected material was removed and an equal amount of oxygen injected. The patient was taken out of splints and two days later he was allowed up on crutches. Ten days after the first injection of oxygen the knee was again aspirated and approximately 30 c. c. of fluid was removed and a like amount of oxygen was left in. The patient was able to return to work in one month, without any loss of motion.

A majority of the cases that have been treated are of the knee joint. However, the ankle, shoulder, elbow, wrist, and the joints of the finger have been treated in the manner heretofore described.

SUMMARY

The injection is done under local anesthesia.

No accident of any nature has occurred and no case has shown any harm from the treatment.

The ages of the patients range from 15 months to 67 years.

The author advocates the method, first, in the acutely injured joint; second, in the joints where long immobilization is required in splints and casts; and third, in acutely inflamed joints.

The author believes that oxygen hastens the absorption of the residues of infection and injuries from the joint, and in some cases there is every evidence that oxygen exerts germicidal powers and combats infection.

The paper is based on a series of one hundred and fifty cases.

DISCUSSION (*Abstract*)

Dr. J. Albert Key, St. Louis, Mo.—I discussed this paper in 1925, or at least Dr. Henson's paper, and at that time it is my impression he was using the oxygen in order to get rid of adhesions which had already formed. At that time I could not see any rhyme or reason to the method, and I told him so. I still do not see how putting oxygen in the joint is going to get rid of adhesions. There must be something to it; otherwise, he would not still be using it.

In prevention of adhesions I think it may possibly have some effect. I do not know. I have not used it. I used oxygen in gonorrheal joints some years ago. I could not see that it made any difference.

I hope sometime he will give a detailed report of a series of cases so we can know the type of joint in which this appears to work.

Dr. Guy W. Leadbetter, Washington, D. C.—I should like to rise in defense of this procedure. In my opinion there are certain definite cases in which it is indicated. In the first place, we have used it now for several years in acute gonococcal joints with a

great deal of satisfaction because of the early relief of pain, and also a definite diminution in the period of length of time of rest and, therefore, a quicker restoration to painless function of the knee, with fewer of the limiting conditions which we often found.

We have found it to be most satisfactory in acute streptococcal joints. We have used it also in some traumatic joints, particularly in that type of traumatic joint which even after you have aspirated it and relieved the tension, immediately fills up again, in spite of any type of bandaging or fixation, and continues to do so as often as it is aspirated.

There is much to be learned about the question of air or oxygen in a joint. First, there is a place for it diagnostically. Not only from the x-ray standpoint is that true, but also from the standpoint of the function of the synovial membrane or whatever the absorptive mechanism of a joint is. I have observed that if you inject an ordinarily mildly traumatic joint, and we have run control cases in that respect, the oxygen is completely absorbed in forty-eight hours, completely gone; but if you inject other joints that have some chronic condition (you are a little uncertain of the diagnosis), you will find that oxygen sometimes will remain a week. You are able to obtain the gurgling of the fluid through the gas; you are able to get the tympanitic note of the oxygen. I think also that oxygen has a definite effect if any organisms are in the closely allied tissues. They may or may not be floating around in the joint. Sometimes you can obtain them from the joint fluid more often than in the periarticular tissues.

I think also it has an inhibiting effect on these organisms.

Finally, I think it has a definitely stimulating effect in speeding up the metabolism of the synovial membrane. In my opinion, it is a form of therapy and diagnosis that should be investigated, probably in the laboratory.

Dr. Henson (*closing*).—A large majority of cases treated are private patients and before considering oxygen treatment a thorough check is made, and only those in whom improvement is a reasonable expectancy are subjected to the injection. There has been no desire on my part to create a large series of injections merely for statistical purposes.

Frequent injections are to be done if desirable results are to be expected. The oxygen in many cases of injection lasts five to ten days. Filtered air lasts even longer in a markedly thickened capsule. In the acutely infected joint relief from pain is evident, because patients ask for the second treatment.

May I repeat that in the acutely infected joint, and the severely injured joint, frequent oxygen injections prevent adhesions. One may feel free to immobilize fractures in and around joints over a longer period of time if oxygen is used at seven- to fourteen day intervals in the joint involved.

A normal joint's ability to absorb oxygen and air is rather rapid, usually twelve to forty-eight hours, but in a traumatized capsule with its rapid expansion, or in a rapidly thickened capsule of acute infection, an entirely different rate of absorption is noted. I have noted on x-ray plates air pockets as long as fifteen days after a twelve-pound pressure inflation.

In acute gonorrheal synovitis, because the gonococci are slightly anaerobic, treatment by oxygen insufflation with excellent results was first reported by Porter and Rucker in the *Journal of the American Medical Association* of May 4, 1929.

It is my belief that infections of joints other than gonococcal respond favorably to oxygen.

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EDITORIAL DEPARTMENT

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ANTISEPTICS FROM THE SOIL

The conquest of infectious disease has provided an exciting medical chapter since the discovery of sulfanilamide. The subsequently developed sulfapyridine and sulfathiazole have greatly widened the field of this class of drugs, since they are active against diseases not affected by sulfanilamide. Sulfathiazole, according to recent evidence, is possibly effective against staphylococci and certain of the colon-typhoid group of organisms.[1,2]

An interesting development is the recent work of Dubos,[3] of the Rockefeller Institute for Medical Research, on antibacterial substances which may be obtained from soil. The earth as the beginning and end of all living things, perhaps can provide an enzyme or micro-organisms to disintegrate every living cell.

An enzyme was obtained from a soil bacillus which destroys the capsule of a particular pneumococcus, just as does its specific immune serum, and thus renders the pneumococcus susceptible to phagocytosis in the body. The enzyme thus prepared was exceedingly specific. It was capable of protecting a mouse against 1,000,000 lethal doses of virulent Type III pneumococci, but was ineffective against other types of this organism. It had also some curative effects after inoculation into mice.

Another type of therapeutic agent obtained from soil was much less specific in its properties, and thus perhaps capable of wider use. A bacillus was isolated which produces a toxin very potent against a large group of gram-positive pathogens. The toxin was detected in growth products of the bacillus and purified chemically. A substance was obtained which Dubos calls gramicidin, highly destructive to gram-positive organisms both *in vivo* and *in vitro*. It was both prophylactic and curative against streptococci and pneumococci when injected intraperitoneally into mice. It had no activity if used by any other route. It failed to protect mice if injected subcutaneously, intravenously, or inthamuscularly.

Dubos classifies gramicidin not as an enzyme but as an antiseptic capable of acting at the pH and temperature of the body and effective in minute concentration. It is much less specific than the pneumococcus capsule-dissolving enzyme, since it affects a large group of micro-organisms, paralleling the reaction of the group to the Gram stain. Dubos suggests that study of its activity should yield valuable information regarding the means of discovering new chemotherapeutic agents.

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EFFECT OF HIBERNATION UPON HUMAN BEINGS

Reports on the "freezing" treatment of inoperable cancer[1] have aroused a great deal of interest over the country in the past two years. The patient is of course not actually frozen. He is put under the influence of sedatives and his temperature considerably reduced and maintained at the low level over a period sometimes of several days. Originators of the method offer the hypothesis that embryonic tissues depend

1. Fay, Temple; and Henry, G. C.: Correlation of Body Segmental Temperature and Its Relation to the Location of Carcinomatous Metastasis: Clinical Observations and Response to Methods of Refrigeration. Surg., Gyn. & Obst., **66**:312 (Feb.) 1938.

for their growth upon a definite degree of warmth, and that, like the developing hen's egg, they will die if the incubator goes too low.

Vaughn,[2] of Loyola University in Chicago, has recently employed the technic of Fay and his associates in Philadelphia of lowering the temperature of patients with advanced hopeless malignancy, in the hope of delaying the spread of metastases and relieving pain. Vaughn succeeded in maintaining the temperature of six patients at around 85 degrees for periods which varied from nine to fifty-four hours, with no deaths during the period of hibernation. This is, of course, about 13 degrees below normal. Detailed laboratory studies of the patients were made during their treatment.

As was expected, the pulse rate fell somewhat with the temperature drop. On restoration to normal temperature the pulse rate became greatly elevated, and this was a critical time in the administration of the method. The respiratory rate was little changed during the low temperature period. The basal metabolic rate fell tremendously in three cases. A patient who had a rate of plus forty-five before treatment had a rate of minus thirty-six during hibernation, a fall of 81 points. The nonprotein nitrogen of the blood usually fell, as did the urea nitrogen. The blood sugar rose markedly, perhaps associated with the absence of muscular effort. The bowels did not function, and the amount of urine diminished steadily. The urine temperature was usually several degrees lower than the rectal temperature.

The Chicago worker reports that the method as a treatment even for terminal cancer is quite hazardous, and its value in the relief of pain uncertain. Growth of skeletal metastases was not retarded in the two patients who lived nine months after treatment. Four patients died between twenty-four hours and three weeks after hibernation.

SELECTION OF HEALTH OFFICERS

For several years the Committee on Professional Education of the American Public Health Association has been working to establish educational qualifications for health officers in the United States. The report of this Committee was adopted by the Governing Council of the Association at its last annual meeting. This points out clearly the basic preparation which is desirable for the position of health officer.

It is recommended by the Public Health Association that "Candidates for appointment as health officers should be graduates of approved medical schools who have completed successfully not less than one year of internship in an approved hospital and in addition a course of not less than one year of graduate instruction in a university, leading to a degree in public health." It indicates also that recognition be given to practical experience in public health administration. The American Public Health Association recommends that recognition be given for the professional standing of persons now performing creditable service as health officers.

This is the first time that any association of nation-wide influence has set forth reasonable qualifications for the health officer. This is a progressive step and is highly commended. This report should be of much value to state officials who are responsible for the selection of health officers; also to those who should be guided as to the amount of basic and graduate preparation for such positions; and likewise to the public which needs to be informed as to the training of health officers. Obviously, this progressive step will serve to improve, strengthen and stabilize the official public health agencies throughout the country.

2. Vaughn, Arkell M.: Experimental Hibernation of Metastatic Growths. J.A.M.A., **114**:2293 (June 8) 1940.

TWENTY-FIVE YEARS AGO

From Journals of 1915

Southern Medical Journal Moves to Birmingham.[1]—On July 1 the editorial and business offices of the Southern Medical Journal and the headquarters of the Southern Medical Association were removed from Mobile to Birmingham. It is with profound regret that I announce my removal from Mobile, which has become to me "a spot of all the earth supremely blessed," and whose good people have treated me with greater kindness and more consideration than I have deserved. I believe that Birmingham offers a larger field and a greater opportunity for me in my private work; and since it is very nearly the geographical center of the South and has unusual railroad facilities, which, added to the fact that it is already a large center of population and industry, Birmingham seems to be a most favorable location for the publication of the Southern Medical Journal and for the headquarters of the Southern Medical Association. * * *

Seale Harris, Editor-in-Chief, Southern Medical Journal; Secretary-Treasurer, Southern Medical Association.

1. Editorial. Announcement of Our Removal from Mobile to Birmingham. Sou. Med. Jour., **8**:641, 1915.

Immunization in Arkansas.[2]—The penitentiary commission is adopting measures to protect the health of convicts. Recently Dr. A. Coulter, penitentiary physician, immunized more than 1,200 convicts against meningitis. Fifteen per cent of convicts on the state farm were found to be infected with malaria.

2. Southern Medical News. Ibid., p. 648.

Book Reviews

A Textbook of Physiology. By William D. Zoethout, Ph.D., Professor of Physiology in the Chicago College of Dental Surgery (Loyola University). Sixth edition. 714 pages, illustrated. St. Louis: The C. V. Mosby Company, 1938. Cloth, $4.00.

This is a popular textbook of physiology well adapted to the needs of the college student. It has been kept up to date by frequent revisions. This edition introduces Dr. W. W. Tuttle as co-author. A few new illustrations have been added and the book has been increased by about fifty pages.

Practical Bedside Diagnosis and Treatment. By Henry Joachim, M. D., Chief-of Medicine, Israel-Zion and Beth Moses Hospitals, New York. 828 pages. Springfield, Illinois: Charles C. Thomas, 1940. Cloth, $7.50.

Dr. Joachim has given the medical profession the results of his own experiences as a practitioner in this book. He makes no attempt to cover the medical field or to write of diseases which he has not personally attended. The clinical history and findings as exhibited at the bedside are given paramount recognition, in order to stress the diagnostic features of the disease. Laboratory study is recognized as an adjunct, except in some instances where it is essential to the making of the diagnosis. Pathological conditions of the body are discussed under twelve sections based on anatomical classification. The treatment of the patient and the disease are stressed.

Ker's Manual of Fevers. Revised by Frank L. Ker, B.A. (Cantab), M.B., Ch B. (Edin.), Senior Assistant and Deputy Medical Superintendent, Little Bromwich Hospital, Birmingham. Fourth Edition. 354 pages. New York: Oxford University Press, 1939. Cloth $4.50.

Thirteen infectious diseases causing fever are described in this book. The revision is done by the son of the original author and he has kept his father's style, making only such additions or omissions as have been made necessary by medical progress. Chemotherapy with sulfanilamide has been introduced. Those coming in contact with infectious diseases, especially in contagious hospitals, will find the advice given in this book sound and practical.

Medical Care (A Symposium) Law and Contemporary Problems. Autumn, 1939, Volume VI, No. 4, 186 pages. Durham: Duke University Law School, 1939. Paper 75c.

This symposium consists of fourteen articles which analyze the national health problem and some of the experimental plans that are being tried to solve it. The laws regarding the restrictions of the practice of medicine are examined and legislation now in effect is discussed. Analyses are made of the F.S.A. plan (with conclusions that are not tenable in Alabama), the National Health Bill and also the cost of a disability insurance system. A pertinent contribution, but more factual data are needed.

Surgical Applied Anatomy. By Sir Frederick Treves, Bart. Tenth Edition. Revised by Lambert Rogers, M.Sc., F.R.C.S, F.R.C.S.E., F.R.A.C.S., F.A.C.S., Professor of Surgery, University of Wales. 748 pages, illustrated. Philadelphia: Lea & Febiger, 1939. Cloth $4.50.

For almost six decades this compend has been in the hands of the surgical student. The book has been modernized and revised so that it presents the anatomy of importance to the surgeon briefly and with accuracy.

Pneumoconiosis (Silicosis): The Story of Dusty Lungs. A Preliminary Report. By Lewis Gregory Cole, M.D., Director of Silicotic Research, John B Pierce Foundation, New York City, and William Gregory Cole, M.D., New York City. 100 pages, illustrated. New York: John B. Pierce Foundation, 1940. Cloth $1.00.

A monograph which describes the work of the authors on the inhalation of mineral dusts. They have examined dust-laden lungs by palpatation and inspection, macroscopically, microscopically and roentgenologically. Four types of dusty lungs are described as the fundamental types, although all may coexist in the same lung. They conclude that 90 per cent of the cases of silicosis are not compensable and that the other 10 per cent should be. The appendix contains two reprints of the writers. A very interesting study.

Population, Race and Eugenics. By Morris Siegel, M.D. 206 pages. Published by the Author, 546 Barton Street, East Hamilton, Ontario, 1939. Cloth $3.00.

This author brings out the present trends in hereditary disorders and defects. He points out that in some, as Huntington's chorea, fragilitis ossium and hemophilia, the mode of transmission has been found, while in other conditions it is not so apparent. These hereditary diseases and defects seem to be on the increase due to the small families of the more intelligent and successful people. The various conditions are discussed which are classified as hereditary defects, and a critique is given of the restrictive measures which have been advocated or made into law.

Trapping the Common Cold. By George Sanford Foster, M.D. 125 pages. New York: Fleming H. Revell Company, 1940. Cloth $1.25.

"Millions upon millions of microbes riding about on airplanes (dust particles) crowd the air we breathe." And to keep from taking cold the writer advises water by the glassful, copiously; exercise, diet, posture, proper environment, humidity and clothes. The routine of living reminds us of Angela Tewksbury Fisher's poem, "Methuselah," which ends,

> "But who on earth would wish to live
> Almost a thousand years?"

Ways to Community Health Education. By Ira V. Hiscock, Professor of Public Health, Yale University School of Medicine, with the Collaboration of Mary P. Connolly, Detroit Department of Health; Marjorie Delavan, Michigan Department of Health; Raymond S. Patterson, John Hancock Mutual Life Insurance Company; and William H. F. Warthen, Baltimore Department of Health. 306 pages, illustrated. New York: The Commonwealth Fund, 1939. Cloth $3.00.

This book answers the question of the health worker as to how to get his message across to the public. The main emphasis is laid on education rather than law enforcement. Suggestions are given for the use of every available means of publicity, as newspapers, pamphlets, radio, exhibits, motion pictures and public meetings. The book tells how to conduct campaigns for health and safety, against diphtheria, tuberculosis, syphilis, and to teach people to live. It is a very helpful book.

The Care of a Small Rat Colony. By Rolland J. Main, Ph.D., Department of Physiology and Pharmacology, Medical College of Virginia, Richmond. Vitamin Assay Laboratory, Department of Agriculture and Immigration, Commonwealth of Virginia. 101 pages, illustrated. St. Louis: The C. V. Mosby Company, 1939. Cloth, $2.00.

This is an eminently practical book for anyone who is doing research work involving the use of rats. There is a detailed discussion of such practical matters as equipment, temperature regulation, food, apparatus for feeding, cages, the most economical methods of caring for the animals, breeding, the diseases of rats and also a discussion of the use of rats for certain assays. Although relatively few readers of this journal will have need for such a book, those who do need it will find it quite valuable. It can be heartily recommended to anyone who is doing research work with rats.

Community Health Organization: A Manual of Administration and Procedure Primarily for Urban Areas. Edited by Ira V. Hiscock, Professor of Public Health, Yale University School of Medicine. Third Edition. 318 pages. New York: The Commonwealth Fund, 1939. Cloth $2.50.

This book is now in its third edition and serves as a useful guide for the balanced planning of public health work in a community. During the past seven years many changes have been made in community health organization due to the increased interest of public officials and the Federal Government. Practically all the chapters have been rewritten and new information has been added. It is a valuable handbook for health officers and the teachers of public health.

Proceedings Tenth International Congress of Military Medicine and Pharmacy, Washington, D. C., May 7 to 19, 1939. Volume Two. 303 pages, illustrated. Washington, D. C. Superintendent of Documents, 1939. Paper 50c.

The proceedings contain a resume of the registration, program and verbatim reports of the various topics which were discussed at the Congress. There is a symposium on "The Role of Aviation Medicine and the Development of Aviation," and the discussions of five questions of military importance, including the medical service of colonial expeditions and the calculation of the number of casualties in war. The medical corps officer will find these reports interesting, whether in the regular army or reserve.

Supervision in Public Health Nursing. By Violet H. Hodgson, Supervisor, Outpatient Tuberculosis Nursing, New York State Department of Health; Formerly Assistant Director, National Organization for Public Health Nursing. 376 pages. New York: The Commonwealth Fund, 1939. Cloth $2.50.

This book, which has been written especially for the supervisor, tells of her duties, how the nurse should plan her work, why supervision is necessary, how to organize the field, the importance of teaching, field visits, the making of records and reports and the reasons why they should be made, the selection of new nurses and volunteers, the value of lay committees, school and industrial work and finally the evaluation of the service rendered. It is an excellent book that should be in the hands of every public health supervisor of nurses.

The Participation of Medical Social Workers in the Teaching of Medical Students. Prepared by Harriett M. Bartlett for the Education Committee of the American Association of Medical Social Workers, Chicago, 1939. 64 pages. Menasha, Wisconsin: George Banta Publishing Company, 1939.

This is a successful effort to show the relationship of the medical social worker to the teaching of medical students. The subject is approached by a review and practical analysis of the teaching of social aspects of medical problems in eleven medical schools in which some type of systematic effort has been made. The objectives are very well formulated and emphasis is placed on the conclusion that the physician in the clinic must initiate, direct and correlate any teaching which is undertaken. The report will be of interest and value to any medical teacher who feels it his duty to present more than the facts of medicine to his students.

Southern Medical News

SOUTHERN PEDIATRIC SEMINAR

The Southern Pediatric Seminar will hold its twentieth annual session at Saluda, North Carolina, July 15-27. The Seminar is "a postgraduate summer course in methods of diagnosis, prevention and treatment of diseases of children." The faculty this year will be made up of thirty-three outstanding physicians in their line of work in the South. Saluda is "in the Land of the Sky," in the very heart of the Blue Ridge Mountains—an ideal place for such a teaching facility as the Seminar. Dr. Samuel F. Ravenel, Greensboro, North Carolina, is Dean; Dr. Frank H. Richardson, Brooklyn, New York and Black Mountain, North Carolina, is Vice-Dean; and Dr. D. Lesesne Smith, Infants' and Children's Sanitarium, Saluda, North Carolina, is Registrar. For program and further information, address the Registrar.

ALABAMA

A series of postgraduate lectures in internal medicine opened in Montgomery recently to continue for six weeks for the benefit of physicians in Montgomery, Bullock, Autauga, Elmore and Lowndes counties. Dr. William A. Sodeman, Instructor in Medicine, and Dr. Julius L. Wilson, Associate Professor of Medicine, at Tulane University of Louisiana School of Medicine, New Orleans, will deliver the lectures. It is planned to give the same lectures in Dothan, Troy, Eufaula and Greenville.

Dr. Emmett B. Carmichael, faculty member at the University of Alabama School of Medicine, Tuscaloosa, recently acted as installing officer when Ohio State University's Pre-Medical Club

Continued on page 34

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Continued from page 782

was formally installed as a chapter of Alpha Epsilon Delta. Dr. Carmichael is National Councilor of the fraternity.

DEATHS

Dr. William Angelo Sparks, Birmingham, aged 64, died March 29.

Dr. Julius Jesse DuBose, Maplesville, aged 70, died April 7 of adenoma of the prostate and bronchopneumonia.

Dr. William Pinson Roberts, Dothan, aged 67, died March 7.

Dr. Paul Stearns Mertins, Montgomery, aged 63, died April 10 of cerebral hemorrhage, uremia and hypertension.

Dr. Frank S. Twitty, Columbia, aged 70, died April 30 of cerebral hemorrhage and arteriosclerosis.

ARKANSAS

The Johnson County Medical Society held its annual banquet session in Clarksville recently with Dr. James M. Kolb, Clarksville, acting as toastmaster and Dr. Raymond Cook, Little Rock, delivering the principal address.

The Independence County Medical Society has appointed the following committee on Cancer Control: Dr. V. D. McAdams, Cord; Dr. E. M. Gray, Mountain Home; and Dr. O. J. T. Johnston, Batesville.

Dr. Henry G. Hollenberg, Little Rock, won the first leg on the H. King Wade golf trophy, first contested for at the Fort Smith meeting of the Society.

Dr. Lewis Hyatt and Dr. Gerald Blankfort, both of Little Rock, have been appointed to the clinical staff of the University of Arkansas School of Medicine.

Dr. A. A. Blair, Fort Smith, did special work at Johns Hopkins during May.

The Arkansas Hospital Association has elected the following officers: Vice-President, Dr. A. S. Buchanan, Prescott; Secretary-Treasurer, Dr. Raymond T. Smith, Fort Smith.

Continued on page 35

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(See back of this page)

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— RADIOLOGY, *22:* 234, February, 1934

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(See reverse side of this page)

Continued from page 34

Dr. Chas. T. Chamberlain, Fort Smith, has been elected a Fellow of the American College of Physicians.

Dr. Virgil Payne, Pine Bluff, suffered a fracture of cervical vertebrae while returning from the Fort Smith session.

DEATHS

Dr. Henry William Cox, Hot Springs National Park, aged 73, died March 22 of pulmonary tuberculosis.

Dr. Franklin Pierce Vines, El Dorado, aged 62, died April 29 of cerebral hemorrhage.

Dr. Caleb Ewin Witt, Little Rock, aged 78, died April 23.

Dr. Francis M. Reed, Turrell, aged 69, died May 6 after a short illness.

DISTRICT OF COLUMBIA

Dr. William H. Sebrell, Jr., Washington, was recently the recipient of the Mead Johnson and Company's prize awarded to him for the discovery of riboflavin and its use in keratitis.

Dr. Warren F. Draper, Assistant Surgeon General, U. S. Public Health Service, Washington, has been elected President of the Academy of Medicine of Washington.

The Wilhelmina C. Hartmann Memorial Wing of the Washington Home for Incurables was formally opened on April 16. Dr. Warfield T. Longcope, Physician-in-Chief of Johns Hopkins Hospital, Baltimore, gave the dedicatory address.

The Section on Neurology and Psychiatry, Medical Society of the District of Columbia, recently elected the following officers for the coming year: Chairman, Dr. Paul Ewerhardt; Vice-Chairman, Dr. Philip Litwin; Secretary-Treasurer, Dr. Isadore Rodis, all of Washington.

The Section on Gastro-enterology, Medical Society of the District of Columbia, recently elected the following officers for the coming year: Chairman, Dr. R. Lyman Sexton; Vice-Chairman, Dr. Allen F. Kreglow; Secretary-Treasurer, Dr. Robert Sterling McGrath, all of Washington.

The Section on Ophthalmology and Otolaryngology, Medical Society of the District of Columbia, recently elected the following officers for the coming year: Chairman, Dr. Edward J. Cummings; Vice-Chairman, Dr. Elmer Shepherd; Secretary, Dr. P. S. Constantinople; Treasurer, Dr. John Trinder, all of Washington.

The Washington Academy of Surgery recently elected the following officers for the coming year: President, Dr. William B. Marbury; Vice-President, Dr. Edmund Horgan; Secretary-Treasurer, Dr. Crenshaw D. Briggs, all of Washington.

Dr. Thomas Parran, Washington, began his second four-year term as Surgeon-General of the United States Public Health Service on April 6.

DEATHS

Dr. Lewis Harvie Taylor, Washington, aged 64, died March 30 of coronary occlusion.

Dr. Henry Clarke Coe, Washington, aged 84, died April 20 of heart disease and arteriosclerosis.

Dr. Lyman Jairus Clements, Washington, aged 74, died April 12 of carcinoma of the parotid gland.

Dr. Arthur Camp Stanley, Washington, aged 56, died April 30 of hypertension, uremia and arteriosclerosis.

Dr. Carroll Royer Baker, Washington, aged 55, died April 23 of cerebral thrombosis and arteriosclerosis.

Brigadier General Charles Richard, Washington, aged 86, died April 19.

FLORIDA

Dr. H. Marshall Taylor, Jacksonville, had conferred on him the honorary degree of Doctor of Science by the John B. Stetson University, De Land, at the commencement exercises on June 3.

The Florida Medical Association, Inc., elected the following officers at the recent annual meeting in Tampa: President, Dr. J. Sam Turberville, Century; President-Elect, Dr. Walter C. Jones, Miami; First Vice-President, Dr. John R. Boling, Tampa; Second Vice-President, Dr. Ferdinand Richards, Jacksonville; Third Vice-President, Dr. E. B. Hardee, Vero Beach; Secretary-Treasurer, Dr. Shaler Richardson, Jacksonville.

Continued on page 36

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Continued from page 35

The recently organized Florida Society of Ophthalmology and Otolaryngology has elected the following officers: President, Dr. H. Marshall Taylor, Jacksonville; Vice-President, Dr. Sherman B. Forbes, Tampa; Secretary, Dr. Carl E. Dunaway, Miami.

The Florida Medical Association will hold its annual graduate short course at the George Washington Hotel, Jacksonville, June 24-29.

Dr. R. D. Ferguson, Ocala, was recently named Chairman of the newly formed Marion County Public Health Committee. This Committee is dedicated to promoting the establishment of a full-time county health unit.

Dr. Edward Jelks, Jacksonville, was guest speaker recently at the fourth annual banquet of Alpha Epsilon Delta, honorary pre-medical fraternity, University of Florida.

Dr. Ralph E. Russell, Ocala's medical examiner for the Civil Aeronautics Authority, took a postgraduate course at George Washington University recently in aviation ophthalmology.

Deaths

Dr. Horace Stokes Zernow, Delray Beach, aged 55, was killed March 26 when the automobile in which he was riding was struck by a train.

Dr. Samuel Stith, Pensacola, aged 69, died March 9.

Dr. Thomas Youngman, Coral Gables, aged 59, died March 11.

Dr. Don Duff Campbell, Miami Beach, aged 65, died March 27 of cirrhosis of the liver.

Dr. Ernest Bruce Hatch, Miami, aged 54, died April 2 of coronary thrombosis.

Dr. David Arthur Mills, Zephyrhills, aged 61, died April 23 of cerebral hemorrhage.

Dr. Joseph Richard Sample, Haines City, aged 73, died March 14.

Dr. Robert Y. H. Thomas, Jacksonville, aged 64, died April 14.

GEORGIA

The Georgia State Medical Association elected the following officers for the coming year at the recent Savannah session: President, Dr. Job C. Patterson, Cuthbert; President-Elect, Dr. Allen H. Bunce, Atlanta; First Vice-President, Dr. Julian K. Quattlebaum, Savannah; Second Vice-President, Dr. Marion T. Benson, Jr., Atlanta; Secretary-Treasurer, Dr. Edgar D. Shanks, Atlanta, re-elected. The 1941 meeting will be held in Macon, May 13-16.

Dr. Stuart P. Vandiviere has resigned as Health Commissioner of Americus-Sumter County to accept an assignment for duty with the U. S. Army air corps at Maxwell Field, Alabama. Dr. Henry T. Adkins, Cochran, has been appointed to succeed Dr. Vandiviere.

The following physicians received certificates of merit for their scientific exhibits at the recent annual meeting of the Medical Association of Georgia: First Award, Dr. H. F. Sharpley, Jr., Savannah; Second Award, Dr. M. E. Winchester, Brunswick; Third Award, Dr. Robert B. Greenblatt, Augusta.

Dr. J. Fletcher Hanson, Macon, and Dr. W. P. Harbin, Jr., Rome, have been elected to fellowship in the American College of Physicians.

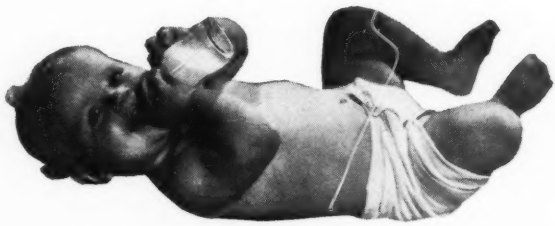
The Medical Staff of the Warren A. Candler Hospital, Savannah, has elected the following officers for the coming year: President, Dr. W. A. Cole, re-elected; Vice-President, Dr. D. B. Edwards; Secretary, Dr. John L. Elliott.

The Second District Medical Society has elected the following officers for the coming year: President, Dr. J. R. Paulk, Moultrie; Vice-President, Dr. Carl S. Pittman, Tifton; Secretary-Treasurer, Dr. J. C. Brim, Pelham.

Dr. A. W. Rehberg, Cairo, has been appointed local surgeon for the Atlantic Coast Line Railroad.

Dr. Ralph Olin Bowden and Miss Margaret Blum, both of Savannah, were married May 3.

Continued on page 38



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Continued from page 36

DEATHS

Dr. Isaac Cuthbert Evans, Jr., Columbus, aged 67, died April 19 of cerebral hemorrhage and arteriosclerosis.

Dr. Lester Lance Lightner, Ideal, aged 57, died April 12 of pneumonia.

KENTUCKY

Dr. Herbert H. Hunt, Mayfield, was recently elected Secretary-Treasurer of the Graves County Medical Society for life. He has served in this capacity for thirty-six years.

Dr. Herman T. Carter, Edmonton, has recently been appointed Director of the Green and Metcalfe counties, a two county health unit.

Dr. Wallace Byrd, Manchester, has been appointed Health Officer of Owen County.

Dr. James W. Scudder, Carlisle, has resigned as Health Officer of Nicholas County.

Dr. Edward C. Humphrey, Somerset, has accepted the position as Health Officer of Mercer County.

Dr. James Levi Thomson, Lexington, and Miss Dorothy Mae Knowles, Woodward, North Carolina, were married May 15.

Dr. Joseph H. Humphert, Covington, and Miss Margaret Jane Leslie, Maysville, were married May 14.

DEATHS

Dr. James Henry Kelley, Flemingsburg, aged 69, died March 22 of pernicious anemia.

Dr. Simon Pendleton Kramer, Fort Thomas, aged 72, died April 12.

Dr. Peter Nicklaus Delus, Louisville, aged 63, died April 7 of uremia.

Dr. Richard M. Jones, Louisville, aged 70, died April 1 of cerebral hemorrhage.

Dr. General Marion Center, Campton, aged 77, died March 5.

Dr. James R. Phillips, Almo, aged 82, died April 7 of pneumonia.

Dr. Emmett Earle Linville, Mount Olivet, aged 57, died April 28 of coronary occlusion.

LOUISIANA

The Louisiana State Medical Society elected the following officers for the coming year at the recent meeting in New Orleans: President: Dr. Christian Grenes Cole, New Orleans; President-Elect, Dr. Paul King Rand, Alexandria; First Vice-President, Dr. H. Ashton Thomas, New Orleans; Second Vice-President, Dr. D. J. Murphy, New Orleans; Third Vice-President, Dr. D. T. Martin, Donaldsonville; Secretary-Treasurer, Dr. Paul T. Talbot, New Orleans, re-elected.

Dr. Lewis C. Spencer, Harrisonburg, has recently been appointed Director of the Vermilion Parish Health Unit with headquarters in Abbeville.

The Louisiana State Pediatric Society has elected the following officers for the coming year: President, Dr. Herman Aubrey White, Alexandria; Vice-President, Dr. Julian Graubarth, New Orleans; Secretary-Treasurer, Dr. William C. Rivenbark, New Orleans.

Dr. Phillips J. Carter, New Orleans, was recently chosen President of the Louisiana Gynecological and Obstetrical Society.

The Franklin Parish Medical Society has elected the following officers for the coming year: President, Dr. J. N. Bostick, Gilbert; Vice-President, Dr. N. E. McElwee, Jr., Crowville; Secretary-Treasurer, Dr. R. E. Applewhite, Winnsboro.

The St. Landry Parish Medical Society has elected the following officers for the coming year: President, Dr. E. L. Landry, Opelousas; Vice-President, Dr. J. J. Stagg, Eunice; Secretary-Treasurer, Dr. S. J. Rozas, Opelousas.

At the annual meeting of the Louisiana Coroners' Association, which was held preceding the meeting of the Louisiana State Medical Society, the following officers were elected: President, Dr. C. Grenes Cole, New Orleans, re-elected; First Vice-President,

Continued on page 40

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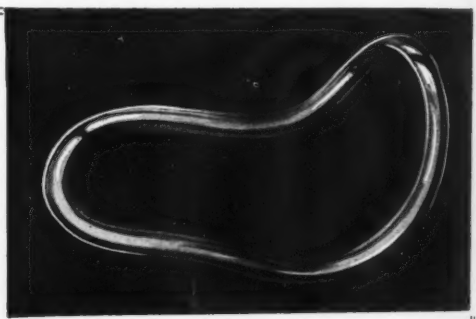

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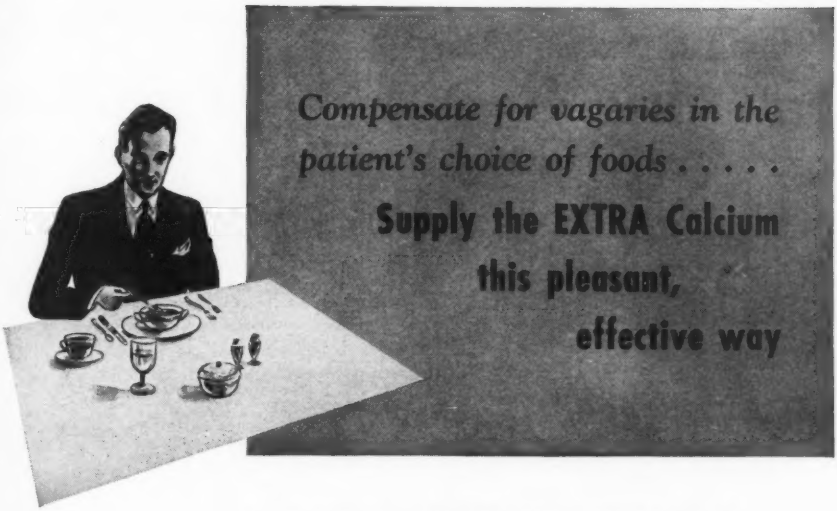

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TABLETS · · · CAPSULES

Continued from page 38

Dr. J. B. Hall, Bossier; Second Vice-President, Dr. C. J. Barker, Thibodaux; Secretary-Treasurer, Dr. L. L. Ricks, Independence.

The Tiger, which has been the official organ of the students of the School of Medicine of Louisiana State University since 1932, has been discontinued. *The Journal of the School of Medicine of Louisiana State University* will be substituted for it.

The George S. Bel Memorial Award, which was given for the first time this year, was presented to James T. Nix, Jr., New Orleans, who recently graduated from the School of Medicine of Louisiana State University.

Dr. Val H. Fuchs, Professor of Otolaryngology in Louisiana State University School of Medicine, has been elected to membership in the American Laryngological Society. Membership is limited to one hundred, and Dr. F. E. LeJeune is the only other member from New Orleans.

Deaths

Dr. John Allen Caruthers, Baton Rouge, aged 64, died April 10 of a fractured hip and arm due to a fall and cerebral hemorrhage and paralysis agitans.

Dr. James Blackman Woodruff, New Orleans, aged 63, died April 22.

Dr. Edwin Rhinehart Yancey, Monroe, aged 53, died March 16.

Dr. John A. Devron, New Orleans, aged 66, died May 13.

MARYLAND

The Finney-Howell Research Foundation, Baltimore, has announced January 1, 1941, as the closing date for the filing of applications for the 1941 awards in cancer research.

Announcement has been made of a grant of $2,000 to Dr. George O. Gey to carry on his work in cancer at Johns Hopkins University School of Medicine.

Dr. Charles E. Gill, formerly of Boston, has been appointed Health Officer of Prince Georges County to succeed Dr. Archie B. Hooton, who recently resigned to go to South Carolina.

Dr. Walter B. Johnson, Cumberland, has been appointed Health Officer of Caroline County with headquarters at Denton.

Dr. Alfred C. Moore, Baltimore, was recently appointed full time medical Health Officer in the Baltimore Health Department. He is the seventh full time officer to be appointed.

Dr. Harvey B. Stone, Baltimore, was recently chosen President of the Medical and Chirurgical Faculty of Maryland to take office January 1, 1941.

Dr. George E. Bennett, Baltimore, was recently chosen President-Elect of the American Orthopedic Association at the meeting in Kansas City.

Deaths

Dr. John Martin Elderdice, Salisbury, aged 61, died April 10 of rheumatic cardiovascular disease.

Dr. Henry Johns Berkley, Baltimore, aged 79, died April 5 of injuries received in a fall.

Dr. Harry Stanton McCard, Baltimore, aged 66, died March 19.

Dr. Henry Castello Foster, Clear Spring, aged 72, died April 29.

MISSISSIPPI

Dr. D. C. Montgomery, Greenville, was elected President of the Louisiana-Mississippi Ophthalmological and Otolaryngological Society.

Deaths

Dr. Josiah S. Wheeler, Tishomingo, aged 75, died March 27 of cerebral hemorrhage and hypertension.

Dr. Junius Taylor Ireys, Greenville, aged 64, died March 31 of chronic interstitial nephritis and arteriosclerosis.

Dr. Clarence V. Gilmore, Hickory, aged 69, died April 3 of pneumonia.

Continued on page 42

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Continued from page 40

Dr. George Thomas Tub, Aberdeen, aged 71, died in April of carcinoma of the liver.

Dr. William Edward Segrest, Sardis, aged 64, died April 10 of cerebral hemorrhage and arteriosclerosis.

Dr. Zealander E. Crawley, Columbia, aged 65, died April 10 of uremia.

MISSOURI

The Missouri State Medical Association elected the following officers for the coming year at the recent annual meeting in Joplin: President, Dr. Cyrus E. Burford, St. Louis; President-Elect, Dr. R. B. Denny, Creve Coeur; Vice Presidents, Dr. L. J. Schofield, Warrensburg; Dr. William J. Stewart, Columbia, and Dr. Paul W. Walker, Joplin; Treasurer, Dr. Ralph L. Thompson, St. Louis.

Dr. Mary Jeannette Lower, Kansas City, was recently presented with the Award of Honor of the Soroptimist Club at a banquet in her honor. The Soroptimist Club is made up of Professional and Executive Business Women.

The annual lectures sponsored by the St. Louis Trudeau Club were recently delivered by Dr. Hyman I. Spector, whose subject was "Differential Diagnosis in Hemorrhage from the Lung," and Dr. Evarts A. Graham, whose subject was "Surgical Aspects of Hemorrhage from the Lung."

The Ellis Fischel State Cancer Hospital at Columbia was recently officially opened. It is said to be the "first hospital ever established by a state for the exclusive care of cancer sufferers."

Dr. E. Lee Dorsett, St. Louis, was elected President of the St. Louis Gynecological Society at the April meeting and Dr. Joseph A. Hardy, Jr., St. Louis, was elected Secretary.

Deaths

Dr. Amalie Marie Napier, St. Louis, aged 73, died March 16 of lobar pneumonia.

Dr. Elisha Herman Liston, Nevada, aged 69, died March 29 of atrophic cirrhosis of the liver.

Dr. Julius Hauck, St. Louis, aged 67, died March 30 of heart disease.

Dr. Michael Pinckney Morrell, St. Louis, aged 89, died March 28 of uremia.

Dr. James Harrison Murphy, Kansas City, aged 77, died March 10 of uremia and arteriosclerosis.

Dr. Charles Augustus Orr, Excelsior Springs, aged 67, died March 11 of duodenal ulcer.

Dr. Archibald Carter Long, Sheridan, aged 70, died March 28 of pulmonary edema and arteriosclerotic heart disease.

Dr. John Kay, Perrin, aged 70, died March 15.

Dr. Otto B. Ilch, Hamburg, aged 71, died April 12 of carcinoma.

Dr. Harold Philipp Kuhn, Kansas City, aged 59, died April 15 of malignant hypertension and chronic nephritis.

Dr. John A. Mann, Wellington, aged 88, died April 20 of hemorrhage of the bladder.

Dr. Mitchell C. Shelton, Joplin, aged 72, died April 24 of coronary occlusion.

Dr. Maurice G. Slocum, Kansas City, aged 65, died April 12 of cardiac decompensation.

Dr. Emile R. Paillou, St. Louis, aged 75, died April 26 of hypostatic pneumonia.

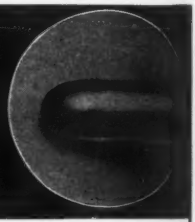
NORTH CAROLINA

Dr. F. Webb Griffith, Asheville, was chosen President-Elect of the Medical Society of the State of North Carolina at the recent Pinehurst meeting.

Dr. Wilburt C. Davison, Durham, Dean of Duke University School of Medicine, recently delivered an address at the dedication of the new buildings for the Lynchburg General Hospital.

Continued on page 44

RADON SEEDS



FOR safety and reliability use composite Radon seeds in your cases requiring interstitial radiation. The Composite Radon Seed is the only type of metal Radon Seed having smooth, round, non-cutting ends. In this type of seed, illustrated here highly magnified, Radon is under gas-tight, leak-proof seal. Composite Platinum (or Gold) Radon Seeds and loading-slot instruments for their implantation are available to you exclusively through us. Inquire and order by mail, or preferably by telegraph, reversing charges.

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SCHERING CORPORATION BLOOMFIELD, NEW JERSEY

Continued from page 42

At the last meeting of the Association of American Physicians held in Atlantic City recently, it was announced that the Kober medal for 1941 would be awarded to Dr. William de B. MacNider, Chapel Hill, for his work in experimental nephritis and in tissue changes and resistance.

Dr. G. M. Cooper, Assistant State Health Officer, and Director of the Division of Preventive Medicine, was presented with a silver inkstand, the gift of associates in the Department on the occasion of the twenty-fifth anniversary of his coming with the State Board of Health.

Dr. David E. Plummer, Mocksville, Director of the Venereal Disease Clinic, Durham City-County Health Department, has been appointed Assistant Professor of Clinical Syphilology in the Division of Public Health, University of North Carolina.

Dr. Logan Everett Sawyer, Durham, and Miss Winifred Lontz Maxwell were married April 28 in Clarksburg, West Virginia.

Classified Advertisements

RATES for insertion in the Classified Column are as follows: $2.00 minimum, which includes the first 50 words; for each word in addition to the original 50 words, the charge is 3c.

WANTED—Southern location in town having open hospital or will consider association with established man doing surgery, or might consider purchase of small going private hospital. Am American, aged 40, well graduated and trained. Experienced general practice and general surgery. Address Box 163, Wolcottville, Indiana.

MODERN WELL EQUIPPED CLINIC-HOSPITAL for sale, reasonable price. Located on U. S. highway, in a good town of 2,500 inhabitants, near large gas field in Oklahoma; failing health main reason for selling. Dept. S-51, SOUTHERN MEDICAL JOURNAL, Birmingham, Alabama.

ASSISTANCE OFFERED TO MEDICAL WRITERS. Research. Abstracts. Translations (all languages). Papers prepared from author's data. Ten years' experience with leading physicians and appointments on medical journals of highest standing. I employ no assistants; all my work is done personally and is reliable. Florence Annan Carpenter, 2220 20th Street, N.W,, Washington, D. C.

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DEATHS

Dr. James Wallace Campbell, Gastonia, aged 69, died March 20 of carcinoma of the liver.

Dr. Eugene Spencer Clark, Clarkton, aged 51, was killed March 11 when struck by an automobile.

Dr. Howard Johnson Combs, Elizabeth City, aged 45, died March 30 of pneumonia.

Dr. Edward Routh Hines, Rocky Mount, aged 59, died April 3 of ruptured esophageal varix with cirrhosis of the liver.

Dr. John Hill Tucker, Charlotte, aged 62, died April 21 of carcinoma of the superior mediastinum.

OKLAHOMA

Dr. J. S. Fulton, McAlester, was honored by the South Eastern Medical Society recently on the anniversary of his fiftieth year in the practice of medicine. He was presented with a beautiful bronze plaque which bore the following inscription: "Joseph Samuel Fulton, M.D., 1890-1940. Fifty years of service to Humanity and Organized Medicine."

The South Eastern Medical Society has elected the following officers for the coming year: President, Dr. W. A. Tolleson, Eufaula; Vice-President, Dr. E. D. Greenberger, McAlester; Secretary-Treasurer, Dr. W. H. Kaiser, McAlester.

Dr. Alpha L. Johnson, El Reno, recently did postgraduate work at the Post-Graduate School of Medicine, New Orleans, Louisiana.

Dr. Roy E. Newman, Shattuck, has gone to Chicago where he will take postgraduate work at the Cook County Graduate School of Medicine.

Dr. Waldo B. Newell, Enid, recently returned from New York City where he spent three weeks taking postgraduate work at Columbia University.

DEATHS

Dr. William G. Woodard, Oklahoma City, aged 78, died March 30 of cerebral hemorrhage.

SOUTH CAROLINA

DEATHS

Dr. James Thomas Jeter, Santuck, aged 72, died April 12 of prostatic hypertrophy, uremia and chronic cystitis.

Dr. Edmund Johnson, Jr., Anderson, aged 58, died April 21 of diabetes mellitus.

TENNESSEE

Dr. Harrison H. Shoulders, Nashville, was unanimously re-elected Speaker of the House of Delegates of the American Medical Association at the recent annual session in New York.

DEATHS

Dr. Rufus E. Fort, Nashville, aged 68, died March 22 of coronary occlusion.

Dr. William Gaylor, Jellico, aged 73, died March 13 of chronic nephritis.

Dr. Robert E. Johnson, Lebanon, aged 83, died March 29.

Dr. Peter Winston Prather, Woodland Mills, aged 61, died April 14 of coronary thrombosis.

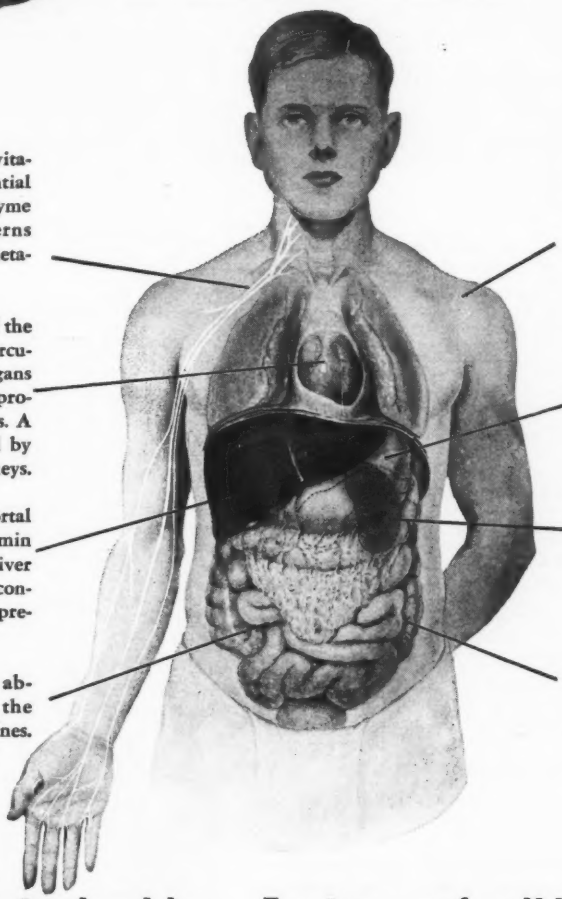
Dr. William Hermann Schultz, Cleveland, aged 66, died April 28 of coronary occlusion.

Dr. Worchester Allen Bryan, Nashville, aged 66, died April 30 of coronary occlusion.

Continued on page 46

STUDIES IN THE AVITAMINOSES

This page is the seventh of a series on vitamin deficiencies presented by the research division of The Upjohn Company because of the profession's widespread interest in the subject. A full color, two-page insert on the same subject appears in the June 22 issue of The Journal of the American Medical Association.



(4) In nerve tissue, vitamin B_1 is an essential component of an enzyme system which governs one phase of the metabolic process.

(3) The remainder of the vitamin enters the circulation, the various organs removing thiamin in proportion to their needs. A large amount is used by heart, liver, and kidneys.

(2) By way of the portal circulation the vitamin is carried to the liver which under normal conditions retains an appreciable amount.

(1) Vitamin B_1 is absorbed from both the large and small intestines.

(5) In skeletal muscle, vitamin B_1 also forms a part of an essential enzyme system governing a phase of the oxidative process.

(6) The secretory and motor function of the stomach may be affected by involvement of the gastric nervous mechanism as a result of B_1 deficiency. This may account for the anorexia in this condition.

(7) If excessive quantities of vitamin B_1 are ingested and absorbed, they are not stored for future use but are excreted by the kidneys; during periods of diuresis considerable quantities of the vitamin may be lost.

(8) Vitamin B_1 found in the feces is largely the result of bacterial growth. Coprophagy provides a source of B_1 for some species of animals.

The Metabolic Fate of Vitamin B_1

In the tissues, vitamin B_1 is an essential part of an enzyme system governing one phase of cellular metabolism. Vitamin B_1 appears to be converted to co-carboxylase, which is essential for the oxidation of pyruvic acid, one of the intermediary products of carbohydrate metabolism.

UPJOHN

Continued from page 44

TEXAS

The State Medical Association of Texas elected the following officers for the coming year at the recent session in Dallas: President, Dr. Preston Hunt, Texarkana; President-Elect, Dr. Neil D. Buie, Marlin; Vice-Presidents, Dr. George A. Schenewerk, Dallas; Dr. James J. Gorman, El Paso; Dr. S. J. R. Murchison, Fort Worth; Secretary, Dr. Holman Taylor, Fort Worth, re-elected; Treasurer, Dr. Khleber H. Beall, Fort Worth. The 1941 session will be held in Fort Worth.

The Texas State Heart Association has elected the following officers for the coming year: President, Dr. K. H. Beall, Fort Worth; Vice-President, Dr. Ghent Graves, Houston; Secretary-Treasurer, Dr. Victor E. Schulze, San Angelo.

The Texas Allergy Association has elected the following officers for the coming year: President, Dr. Boen Swinny, San Antonio; Secretary, Dr. Homer Prince, Houston.

The Texas Dermatological Society has elected the following officers for the coming year: President, Dr. W. A. Smith, Beaumont; Vice-President, Dr. J. Lewis Pipkin, San Antonio; Secretary, Dr. D. O. Poth, San Antonio.

The Texas Orthopedic Association has elected the following officers for the coming year: President, Dr. W. B. Carrell, Dallas; Vice-President, Dr. E. M. Cowart, Houston; Secretary-Treasurer, Dr. Ruth Jackson, Dallas.

The Texas Society of Gastro-enterologists and Proctologists has elected the following officers for the coming year: President, Dr. M. O. Rouse, Dallas; First Vice-President, Dr. Hugh Welch, Houston; Second Vice-President, Dr. G. E. Brereton, Dallas; Secretary, Dr. Tom E. Smith, Dallas.

The Texas Association of Medical Anesthetists has elected the following officers for the coming year: President, Dr. Thomas H. Compere, Houston; Vice-President, Dr. Frank O. Barrett, El Paso; Secretary-Treasurer, Dr. R. A. Miller, San Antonio.

The Texas Neurological Society has elected the following officers for the coming year: President, Dr. Wilmer L. Allison, Fort Worth; First Vice-President, Dr. William Thomas, Terrell; Second Vice-President, Dr. E. M. Perry, Dallas; Secretary-Treasurer, Dr. Melbourne J. Cooper, San Antonio.

Dr. J. B. Barnett has removed from Thornton to Marlin.

Dr. Wheeler Bell has removed from San Antonio to Warrington, Florida.

Dr. Paul V. Colvin has removed from Longview to Kelly Field.

Dr. Arlin B. Cooper has removed from San Marcos to Bee Wheeler.

Dr. Clarence Edens has removed from San Marcos to Tyler.

Dr. B. H. Estess has removed from New Braunfels to Austin.

Dr. Joseph L. Hall has removed from Roscoe to Stanton.

Dr. John M. Hooper has removed from Baltimore, Maryland, to McKinney.

Dr. James R. Jeter has removed from Sherman to Ennis.

Dr. D. H. Kaump has removed from Temple to Detroit, Michigan.

Dr. H. O. Padgett has removed from Graham to Dallas.

Dr. George F. Rozelle, Jr., has removed from Fort Worth to Trudeau, New York.

Dr. A. L. W. Tackaberry has removed from New Waverly to Humble.

DEATHS

Dr. Robert Lee LaRue, Eustace, aged 70, died March 20 of pneumonia.

Dr. Moses Sylvester Howell, Greenville, aged 77, died March 8.

Dr. Grace Hovey Griffin, Houston, aged 54, died April 2 of chronic lymphatic leukemia.

Dr. Hugh Wilmer Duke, Amarillo, aged 66, died March 23 of chronic myocarditis.

Dr. Donnell Bone Braly, Troup, aged 63, died April 21 of myocarditis.

Dr. John S. Yates, Rosenburg, aged 75, died April 6 of congestive heart failure and chronic nephritis.

VIRGINIA

The annual meeting of the Virginia State Medical Society will be held jointly with the annual meeting of the West Virginia State Medical Society at the Greenbrier Hotel, White Sulphur Springs, West Virginia, July 29-31.

The Virginia Society of Ophthalmology and Otolaryngology at the recent meeting at Old Point Comfort elected the follow-

Continued on page 48

HEAT
WILT
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This balanced mineral water replenishes essential salts and water lost through excessive perspiration. It tends to inhibit fatigue, muscle soreness and collapse due to excessive exercise at high temperatures. Literature on request.
WHEN IT'S BLAZING HOT
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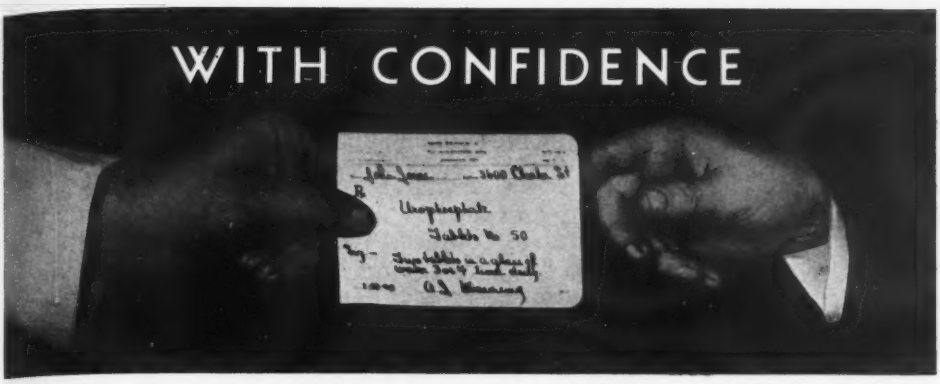

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EFFECTIVENESS

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URO-PHOSPHATE in proper dosage is a complete treatment—the acidifying drug necessary for the liberation of formaldehyde is contained in the tablet with the methenamine.

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DOAK CO., INC.
CLEVELAND, OHIO

Continued from page 46

ing officers for the coming year: President, Dr. George G. Hankins, Newport News; Vice-President, Dr. Mortimer H. Williams, Roanoke; Secretary-Treasurer, Dr. Guy Fisher, Staunton. The 1941 meeting will be held in Richmond.

Dr. E. T. Gatewood, Richmond, was made a Fellow of the American Rhinological Society at the recent annual meeting in New York.

The following Virginia physicians were among those inducted into fellowship of the American College of Physicians at the recent Cleveland meeting: Dr. Walter Paul Adams, Norfolk; Dr. Andrew DeJarnette Hart, Jr., University; and Dr. Burbridge Scott Yancey, Harrisonburg.

Dr. P. G. Hamlin, recently connected with the Eastern Shore State Hospital at Cambridge, Maryland, has returned to Virginia and assumed duties as Clinical Director of the Eastern State Hospital at Williamsburg.

Dr. Warren T. Vaughan, Richmond, was recently elected President of the Harvard Club of Virginia.

Dr. A. Tyree Finch, Chase City, has been appointed Health Officer of Chase City.

Dr. Dupont Guerry, of the staff of the Manhattan Eye, Ear and Throat Hospital, New York, has been given the John Horsley Memorial Prize in medicine of $600 in recognition of his discovery of "the use of vitamin K in stopping excessive bleeding in newborn infants." This work was done in association with Dr. William W. Waddell, Jr., Associate Professor of Pediatrics, University of Virginia Department of Medicine, Charlottesville. The fact that he graduated more than fifteen years ago from the medical school made Dr. Waddell ineligible for the prize.

Dr. Edward Marshall Sandidge, Pleasant View, and Miss Nellie Penn McDaniel, Sandidge, were married April 3.

Deaths

Dr. John Lee Grant, Winchester, aged 65, died March 21 of cerebral hemorrhage with hemiplegia.

Dr. Bascom Hugh Birney, Burkes Garden, aged 82, died April 19 of coronary occlusion and arteriosclerosis.

Dr. Asa Wesley Graves, Lacey Spring, aged 61, died April 12 of diabetes mellitus.

Dr. Herbert Augustus Allen, Richmond, aged 55, died April 30 of cerebral hemorrhage.

Dr. Robert Lee Page, Batesville, aged 77, died April 9.

Dr. Thomas Melville Talbott, East Falls Church, aged 91, died May 10 of pneumonia.

Dr. James Wilson Hunter, Jr., Norfolk, aged 62, died May 11.

Dr. Donald MacKenzie Faulkner, Richmond, aged 47, died May 6.

WEST VIRGINIA

The annual meeting of the West Virginia State Medical Society will be held jointly with the annual meeting of the Virginia State Medical Society at the Greenbrier Hotel, White Sulphur Springs, July 29-31.

Dr. George Lyon, Huntington, has been appointed a member of the National Advisory Committee on Maternal and Child Health to the Department of Labor at Washington.

Eight of the ten West Virginia scholarships for the annual two weeks' pediatric seminar at Saluda, North Carolina, have just been announced by the Association's Committees on Maternal and Child Welfare and the State Health Department. These scholarships were awarded to: Dr. W. P. Bittinger, Summerlee; Dr. Fred Ben Quincy, Williamson; Dr. J. A. Streibich, Moundsville; Dr. A. A. Davidman, Logan; Dr. T. O. Snaith, Weston; Dr. S. A. Jacob, Bethany; Dr. A. G. Lanham, Ronceverte; and Dr. W. F. McFarland, Keyser.

The Ohio County Medical Society has elected the following officers for the coming year: President, Dr. J. O. Rankin; Vice-President, Dr. Carl S. Bickel; Secretary, Dr. H. G. Little; Treasurer, Dr. E. N. Pell, all of Wheeling.

Deaths

Dr. William T. Cameron, Mace, aged 73, died April 12 of cerebral hemorrhage.

Dr. William A. Marsh, Green Lawn, aged 79, died April 17 of cerebral hemorrhage.

Dr. Clem C. Ballard, Gap Mills, aged 61, died March 31.

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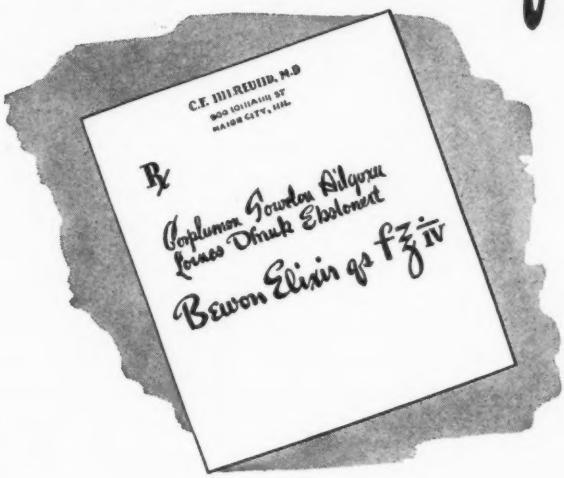

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HIS FIRST CEREAL FEEDING

The baby's first solid food always excites the parents' interest? Will he cry? Will he spit it up? Will he try to swallow the spoon? Far more important than the child's "cute" reactions is the fact that figuratively and physiologically this little fellow is just beginning to eat like a man.

IT is a fortunate provision of Nature that at the time the infant is ready to receive the nutritional benefits of cereal, his taste is unspoiled by sweets, pastry, condiments, tobacco, alcohol and other things to which adult palates and constitutions have become conditioned.

Many a parent, with limited knowledge of nutrition, attempts to do the baby's tasting for him. Partial to sweets, the mother sweetens her child's cereal. Disliking cod liver oil, she wrinkles her nose and sighs: "Poor child, to have to take such awful stuff!" The child is quick to learn by example, and soon may become poor indeed—in nutrition, as well as in mental habits and psychological adjustment.

Appreciating the importance and difficulties of the physician's problem in establishing and maintaining good eating habits, Mead Johnson & Company continue to supply Pablum in its natural form. No sugar is added. There is no corresponding dilution of the present protein, mineral and vitamin content of Pablum. Is this not worth while?

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Take along PABLUM in the new half-pound size

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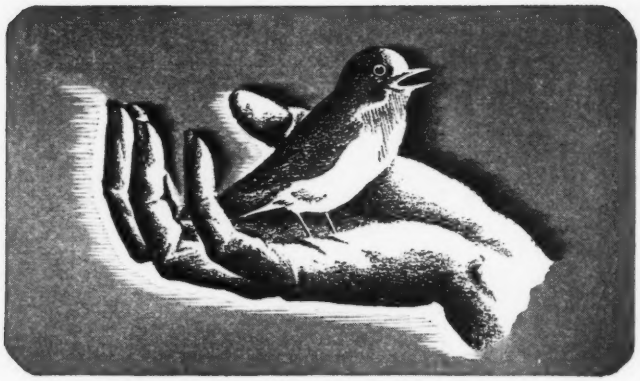
Whether or not there is a baby in your family Pablum is a convenient, nutritious food to include in the vacation kit. This unique cereal can be served in an instant ... almost anywhere, any time. No cooking is required. All that's needed is to add water or milk of any temperature. As a physician you will appreciate the advantage that Pablum, unlike so many camp rations which tend to be concentrated carbohydrate lacking in minerals and vitamins, supplies generous amounts of calcium, phosphorus, iron and vitamins B_1 and G (riboflavin). Its iron and calcium content is far higher than that of bulky, perishable vegetables. Pablum is light and easy to carry, especially in the new ½-lb. package.*

*Pablum is also supplied in an economical 1 lb.-2 oz. package, replacing the former 1 lb. size. A palatable mixed cereal food, Pablum consists of wheatmeal (farina), oatmeal, wheat germ, cornmeal, beef bone, alfalfa, yeast, sodium chloride and reduced iron. • MEAD JOHNSON & COMPANY, EVANSVILLE, IND., U.S.A.



Research philosophy is different

The "bird in the hand" idea may often be sound policy. But research has a different philosophy. It is looking for the "two birds in the bush." The true scientist isn't content with what's already been done. He is deliberately searching into the unknown.

This philosophy has motivated many Parke-Davis contributions to modern medicine. For example—Adrenalin, Pituitrin, Pitocin and Pitressin, Mapharsen, Meningococcus Antitoxin. Each of these has enabled the physician to treat his patients more effectively, more safely, and with more confidence.

This philosophy constantly directs Parke-Davis research toward discovery and development of new and better therapeutic agents.

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